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ABSCESS OF THE BRAIN

RELATION OF THE HISTOLOGIC TO THE CLINICAL FEATURES

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PHILADELPHIA

The formation of an abscess of the brain is so intimately associated with its treatment that the study of the one must inevitably shed light on the other. The reason for this intimate relation of the histologic picture to the treatment lies in the fact that in abscesses of the brain, as in abscesses elsewhere in the body, the most important problem which the surgeon has to solve is when to operate. Shall operation be performed during the acute stages of the illness, when there is much prostration and severe systemic reactions are present, or shall it be delayed until there is evidence of encapsulation of the abscess? The answer to this question in recent times has been almost invariably to delay operation in most cases until encapsulation has been known to occur. This has come to be the surgeon's rule of thumb in the majority of cases of abscess of the brain.

Since encapsulation of the abscess is so important in its treatment, it is obviously desirable to know all that is possible concerning the process of encapsulation and to determine if possible when encapsulation occurs. For this reason I have analyzed 27 cases of histologically verified abscess of the brain specifically with the following questions in mind: 1. How does encapsulation take place? 2. When can it be said to have occurred? 3. What relation does it have to the bacterial content of the abscess? 4. What should be its relation to operation? In other words, should operation wait on encapsulation? Answering these questions, in general, is the task which I set for myself in this study; other problems incidental to these general aspects of the problem of abscess also will be dealt with (table).

HISTOLOGIC FEATURES OF ABSCESS OF THE BRAIN

GENERAL FEATURES

The general features of abscess of the brain have been well worked out, and for this reason will be dealt with only summarily. Homen [1]

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Read at the Sixty-Fourth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 2, 1938.

1. Homen, E. A.: Experimentelle und pathologische Beiträge zur Kenntnis der Hirnabszesse, Arb. a. d. path. Inst. d. Univ. Helsingfors **1**:1, 1913.

Case No.	Age	Sex	Location	Duration of Symptoms	Primary Focus	Organism
1	20	M	Frontal (R)	5 yr. (trauma)	Trauma	Pneumococcus; few Staph. aureus nonhaemolyticus
2	40	M	Parietal (R)	11 mo.	Bullet wound in brain	Staph. aureus nonhaemolyticus
3	7	M	Frontal (L)	3 mo.	Trauma	Pneumococcus type I
4	24	F	Frontal (L)	11 mo.	Sinus—left frontal	Staph. albus haemolyticus
5	13	M	Temporo-frontal (R)	2 wk.	Trauma (bumped head while wrestling); furuncles—series for last 2 mo.	Staph. pyogenes aureus haemolyticus
6	9	M	Occipital (L)	6 mo.	Tonsillectomy; abscess of lung	Str. subacidus (Holman)
7	21	M	Frontal (L)	6 wk.	Series of boils 3 mo. before entrance; sinuses—maxillary; middle ears	Staph. aureus haemolyticus
8	36	M	Cerebellar (R)	3 wk.	Otitis media, bilateral	Pneumococcus type III
9	23	M	Frontal (R)	11 mo.	Trauma	Staph. albus haemolyticus
10	10	M	Frontotemporal (L)	4 wk.	Trauma	Pneumococcus type I
11	10	M	Frontal (R)	4 mo.	Sinuses—ethmoid	Staph. aureus nonhaemolyticus
12	47	M	Frontal-motor (R)	10 wk.	Carbuncle—neck; ischiorectal abscess	Staph. aureus haemolyticus
13	26	M	Frontal (R)	2 mo.	Sinus—sphenoid (R)	Pneumococcus; streptococcus
14	20	M	Frontal (R)	3 mo.	Trauma—osteomyelitis 12 yr. previously; 2 operations for osteomyelitis on bones of skull	Staph. aureus haemolyticus
15	26	M	Frontal (L)	5 days	Mastoid infection 6 mo. previously; mastoid operations 5 mo. and 4 mo. previously	Staph. aureus haemolyticus
16	12½	F	Frontal (R)	6 days	Sinus—frontal (R)	Str. haemolyticus
17	36	M	Frontotemporal (R)	10 days	Sinuses—maxillary and ethmoid	Staph. albus nonhaemolyticus
18	13 mo.	F	Frontal (R)	3 wk.	Encephalocele (frontal); incision; drainage of fluid; meningitis; abscess	Str. haemolyticus predominant; Staph. aureus haemolyticus also from base of skull
19	19	M	Frontal (R)	5 mo.	Sinuses—frontal; submucous resection 9 days before last entrance; osteomyelitis—frontal (R)	Staph. albus haemolyticus and nonhaemolyticus; Staph. aureus haemolyticus
20	30	M	Occipital (L)	2 mo.	Carbuncles 1 year previously; furuncle (boil) on left arm 3 mo. previously	Staph. aureus haemolyticus
21	49	F	Frontal (L)	2½ mo.	Sinus—frontal; osteomyelitis—frontal (L)	Gram-negative rods of achromobacter group (water group)
22	26	M	Frontal (R)	3 mo.	Teeth—abscesses; osteomyelitis—frontal (R); sinus—frontal (R)	Staph. aureus
23	15	M	Cerebellar (R)	3 wk.	Mastoid	Str. subacidus haemolyticus
24	25	M	Frontal (L)	6 wk.	Sinus—frontal (bilateral)	Staph. aureus
25	55	M	Temporal (R)	6 wk.	Mastoid (R)	Str. haemolyticus
26	15	F	Cerebellar (L)	3 wk.	Otitis media (L)	Str. haemolyticus
27	45	M	Temporal (R)	4 wk.	Abscess of lung	Str. haemolyticus

described four layers from within out in the wall of experimental abscess of the brain: (1) an exudative layer, composed of the innermost part of the abscess and containing exclusively necrotic material; (2) an infiltrative layer, composed of a dense connective tissue membrane; (3) a fibrillar layer, composed of new vessels, connective tissue and neuroglial fibrils, and (4) a rarefied layer, composed of edematous brain tissue surrounding the abscess. Midowski [2] described three layers, composed of (1) inflammatory, (2) necrotic and (3) connective tissue. Globus and Horn [3] divided the abscess into: (1) the cavity of the abscess itself, (2) a vascular layer which lies just outside the cavity and (3) a fibrous zone just beyond this.

Study of the cases reported in this paper showed that the abscess is composed of the following layers:

1. *Necrotic Zone (Cavity of the Abscess).*—This portion of the abscess consists of the "core" of the abscess. In recent abscesses it is composed of well preserved polymorphonuclear leukocytes. In older abscesses it consists of necrotic tissue formed by the destruction of polymorphonuclear cells. The nuclei of these cells, often distorted and broken up, lie scattered in a mass of tissue débris formed by the cytoplasm of these cells. In old abscesses small granules of calcium may be seen within the necrotic tissue.

2. *Reactive Zone.*—Adjacent to the necrotic zone is what may be termed the reactive zone. This consists of a layer of loose connective tissue in which lie fibrin vessels and cells of various sorts. The connective tissue in this layer is usually seen with routine aniline stains (hematoxylin and eosin, trichrome) as a loose-meshed collagen structure, the fibrils of which lie in parallel rows. Silver stains (Hortega, Laidlaw), however, reveal a much more complex connective tissue structure than one sees with other stains. With such stains one sees a dense, intertwining mesh of connective tissue in which lie many vessels. The density of this structure is a matter of great surprise, so different is its appearance from the structure of this zone as seen with other stains. The vessels, which are numerous, are chiefly thin-walled veins or capillaries. No proliferative changes are seen in the vessels usually, but they may be present in some instances. Early in the formation of the abscess, fibrin is seen in this zone. Gitter cells also are seen in this layer in early abscesses and may persist even in older abscesses. As a rule, however, these cells are present early in the formation of the abscess only. Polymorphonuclear leukocytes are entwined in the collagen

2. Midowski, F.: Beiträge zur Pathogenese und pathologische Histologie des Hirnabszess, Arch. f. Ohrenh. **77**:239, 1908.

3. Globus, J. H., and Horn, W. L.: Inherent Healing Properties of Abscess of the Brain, Arch. Otolaryng. **16**:603 (Nov.) 1932.

meshes in early abscesses. These are replaced later by lymphocytes and plasma cells. Even when the latter predominate, polymorphonuclear cells may still be seen, though not in great numbers.

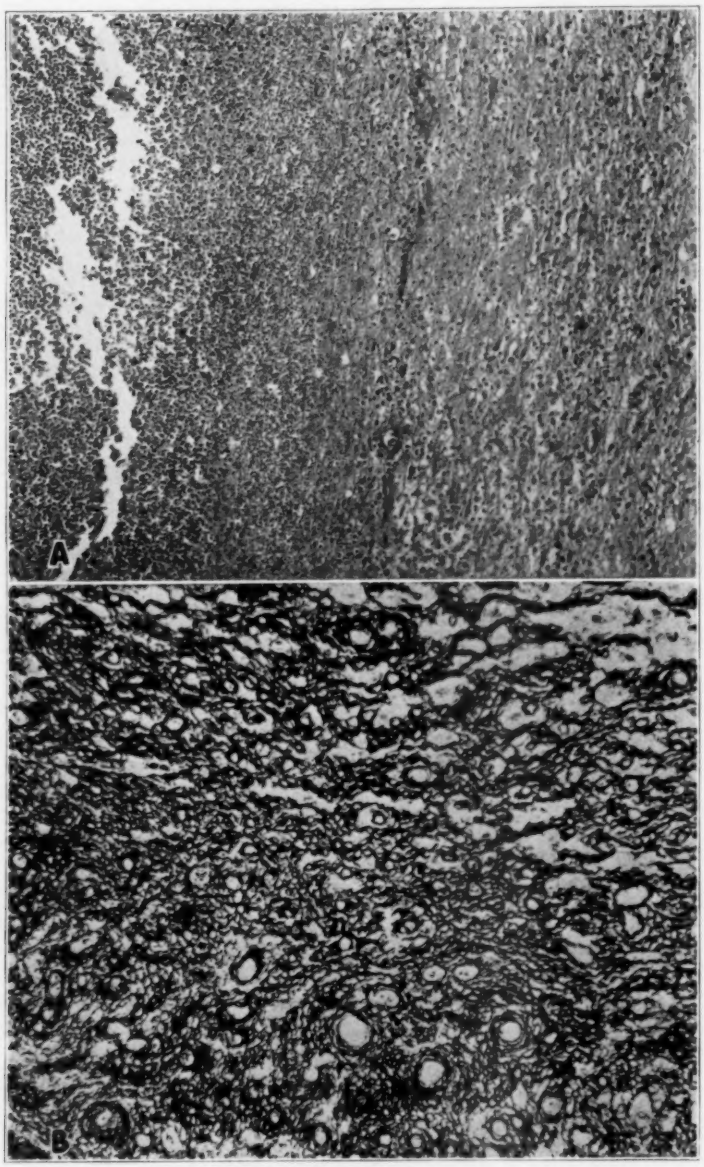

Fig. 1.—An early abscess (five days). In *A* little formation of connective tissue is seen with hematoxylin-eosin stain. In *B*, however, capsule formation is seen in the rich carpet of silver fibers shown by Hortega's silver stain. The etiologic organism was Staphylococcus aureus haemolyticus.

3. *Fibrous Zone.*—Beyond the reactive zone in an abscess with a well developed capsule is what may be termed the fibrous zone. This is composed of a dense layer of fibrous tissue of varying thickness. The bundles of fibrous tissue lie in parallel rows. With trichrome stains they appear to be long, wavy and closely packed and to contain a moderate number of fibroblasts among the collagen bundles. With silver stains the fibrous tissue appears as long, hard fibrils lying in parallel rows. Sometimes lymphocytes or plasma cells are seen among the collagen bundles. There are few vessels in this layer, in contrast to the large number of vessels in the reactive zone.

4. *Encephalitic Zone.*—In some abscesses, outside the fibrous zone is a zone of varying width characterized by changes within the brain tissue itself. This may be termed the encephalitic zone. When present it is usually well marked. It may extend for some distance into the surrounding brain tissue, or it may be confined to a narrow zone immediately surrounding the abscess. Within this zone one sees many cells, both in the brain tissue itself and in the perivascular spaces. These cells are polymorphonuclear leukocytes in the early stages of the disease but later become lymphocytes and plasma cells. They are scattered diffusely in the brain tissue. Perivascular infiltration is pronounced in these areas. The ganglion cells in the adjacent cortex are swollen and show typical toxic ganglion cell changes. The astrocytes are swollen; the oligodendroglia shows evidences of acute swelling, and the microglia also is swollen in the acute stages of the process. In every case the meninges above the abscess show infiltration of a varying degree. This meningeal exudate is usually localized in an area immediately adjacent to the abscess, but it may become generalized and spread through the entire subarachnoid space. The exudate is usually composed of polymorphonuclear leukocytes, but in chronic abscesses it may consist chiefly of lymphocytes and plasma cells.

FORMATION OF ABSCESS OF THE BRAIN AND ITS CAPSULE

The development of an abscess of the brain from its inception has been well studied by Globus and Horn.[3] They stated that the earliest process in the formation of an abscess of the brain consists of a small circumscribed area crowded with bacteria, polymorphonuclear leukocytes, lymphocytes, red blood cells and disintegrating neural elements. In the center of these elements is a blood vessel, which has given rise to the suppuration by thrombosis and subsequent rupture. Several of these foci may be seen lying adjacent to one another. These later coalesce to form a single large suppurative process. The authors said:

> Shortly after the extravasation of the suppurative material from the thrombosed vessel has taken place, reactive phenomena begin to appear at the periphery

of the suppurative process. Numerous small blood vessels appear surrounded by lymphocytic and leukocytic infiltrations. At first the vessels are few in number, forming a well defined belt around the suppurative zone. Then more vessels

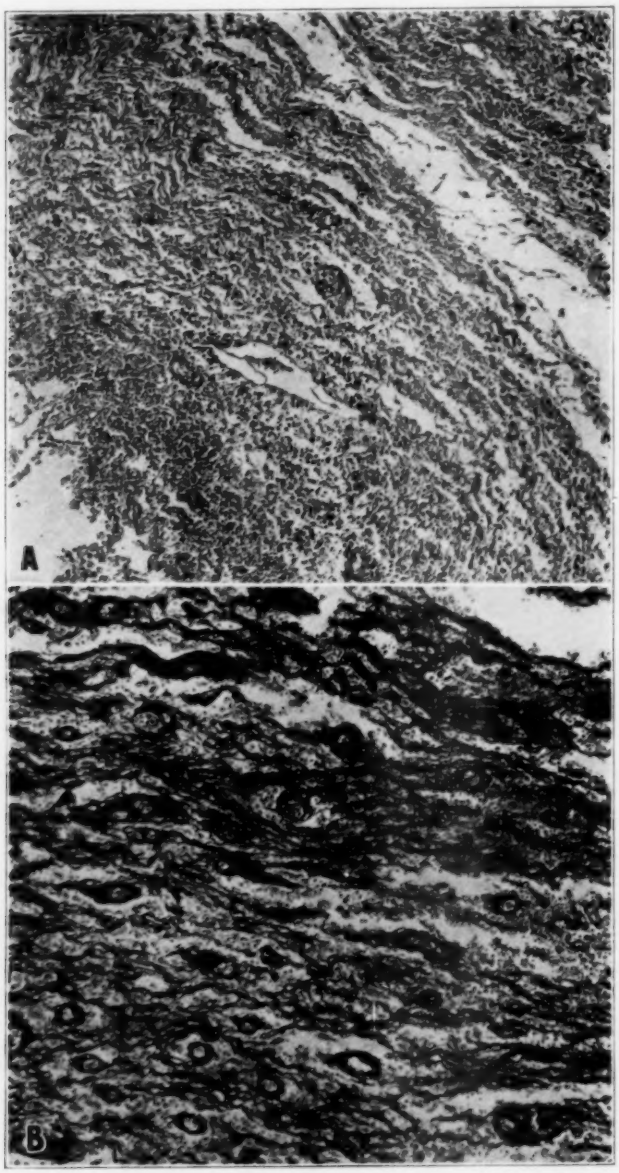

Fig. 2.—An abscess of six days' duration. In *A* delicate strands of fibrous tissue outside the cavity of the abscess are already visible with the hematoxylin-eosin stain. The silver stain (*B*) shows a heavy carpet of fibrous tissue. The organism was Streptococcus haemolyticus.

come into view, forming several rows; the blood vessels enlarge in size, and are surrounded by denser masses of infiltrating elements. Within a brief period of time lymphocytic elements begin to stray away from the perivascular zones, imparting to the surrounding tissue the character of an interstitial lymphocytic infiltration.

These lymphocytes may become converted into fibroblasts.

It seems reasonable now to assume that the migratory lymphocytes provide the material necessary for the construction of the abscess capsule by their conversion into fibroblasts and ultimately into collagenous structures. In the course of time the number of vessels in the area, as well as the number of lymphocytes about the abscess, increases progressively. The fibroblasts become more and more numerous and the collagenous tissue denser, with the result that a well organized limiting membrane . . . is formed.

Development of the Capsule.—Abscesses of the brain, like abscesses elsewhere in the body, become encapsulated in the course of time. This statement is true in general, but it has certain reservations, which will be mentioned later, in the discussion of the relation of capsule formation to the clinical symptoms.

Time of Capsule Formation: One of the most important problems in the question of development of the capsule is the problem of the time necessary. Obviously, if a definite solution can be given to this problem the decision of the surgeon as to the optimum time for operation will be greatly simplified. It should be recognized clearly at the outset, however, that not all abscesses act alike in the development of the capsule as concerns both the time and the type of capsule formed. Capsules have been seen at an early stage in some cases, and not at a similar stage in other cases. This is because the formation of the capsule is dependent on the following variable factors: 1. The nature of the invading organism. Some organisms are more prone to induce capsule formation than others. This point will be discussed in another section. 2. The resistance of the host. This is probably an important factor in the capsule formation, but it is an intangible, which is not easily measured and hence is difficult to evaluate. This view is substantiated by the observations of Atkinson,[4] who found that no capsule was formed after infection by very virulent organisms, the result being only rapidly spreading encephalitis. He found, moreover, that the greater the resistance of the host, the more definite was the possibility of capsule formation.

An additional confusing factor is the fact that the calculation of time in abscess formation is at best a crude one. The onset of an abscess is usually reckoned from the time of onset of symptoms.

4. Atkinson, E. M.: Pathology of Adjacent Brain Abscess, Proc. Roy. Soc. Med. (Sect. Otol.) **23**:55 (May) 1930; Pathology, Diagnosis and Treatment of Brain Abscess, Lancet **1**:483 (March 10) 1928.

Actually this indicates only the time of probable overt invasion of the brain. Quiet invasion may have occurred with only minor symptoms. Moreover, the invasion of the brain may be effectively masked in cases in which the condition is acute and there are severe systemic reactions from acute otitis or sinusitis. In any event the calculation of capsule formation from the time of onset of symptoms furnishes a rough estimate which cannot be regarded as in any sense accurate.

With these factors in mind it becomes obvious that the optimum time for the formation of the capsule of an abscess is variable within wide limits. This is reflected clearly in the various reports which have been recorded from time to time concerning the time of formation of

Fig. 3.—An abscess of ten days' duration in the frontal lobe. It is not encapsulated. Microscopic study shows encephalitis but no capsule formation. The focus was in the maxillary and the ethmoid sinuses, and the causative organism was Staphylococcus albus nonhaemolyticus.

the capsule. Homen [1] observed reparative changes beginning on the fifth to the seventh day in experimental abscesses. Westphal [5] saw evidence of a capsule after ten days and after seventeen days. Lallemand [6] saw a capsule formation after thirteen days and Eagleton [7] after seventeen. Uchermann [8] described a 1 mm. capsule after twenty-four

5. Westphal, A.: Ueber Gehirnabscesse, Arch. f. Psychiat. **33**:206, 1900.

6. Lallemand, C. F.: Recherches anatomico-pathologiques sur l'encéphale et ses dépendances, Paris, Béchet, 1830-1834.

7. Eagleton, W. P.: Brain Abscess, New York, The Macmillan Company, 1922.

8. Uchermann, V.: Otitische Gehirnleiden, Ztschr. f. Ohrenh. **46**:303, 1903.

days, a 1 to 2 mm. capsule after thirty-eight days and a 6 mm. capsule after one hundred and twenty-eight days. Merkens [9] reported a capsule after thirty-one days. Lebert [10] saw capsule formation after three to four weeks, Schatt [11] after seven to eight weeks and Jansen [12] after

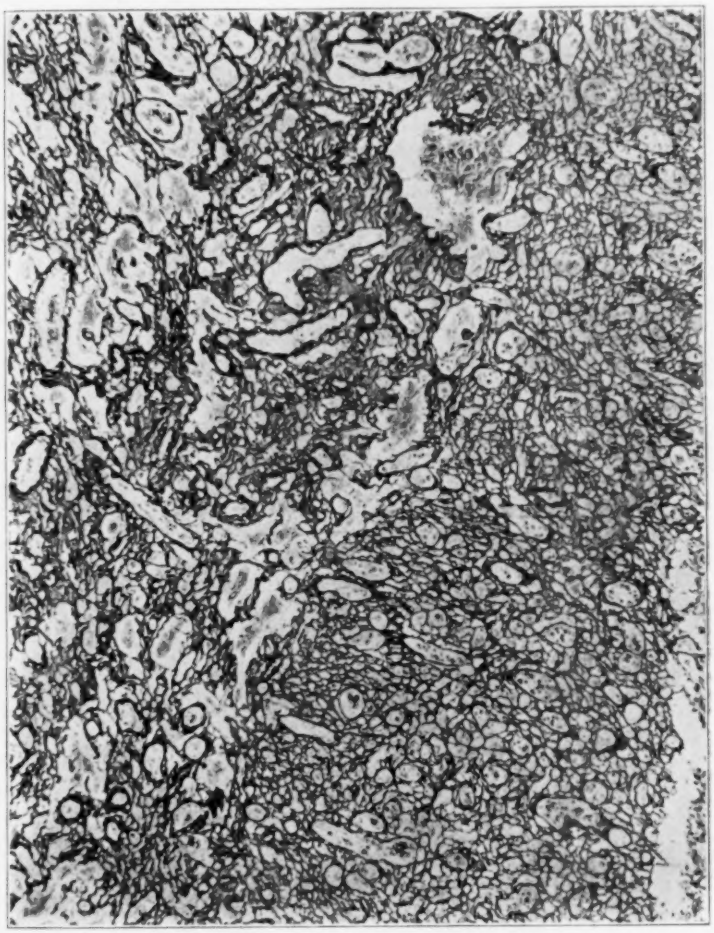

Fig. 4.—An abscess of two weeks' duration (Laidlaw connective tissue stain). Collagenous tissue is already being deposited. The organism was Staph. aureus haemolyticus.

9. Merkens: Ueber intrakranielle Komplikationen bei Mittelohreiterung, Ztschr. f. klin. Chir. **59**:70, 1901.

10. Lebert: Ueber Gehirnabscesse, Virchows Arch. f. path. Anat. **10**:78, 1856.

11. Schatt, cited by Oppenheim, H., and Cassirer, R.: Der Hirnabszess, Vienna, A. Hölder, 1909.

12. Jansen: Ueber otitische Hirnabscesse, Berl. klin. Wchnschr. **28**:1160, 1891.

five weeks. Huguenin [13] saw no capsule at thirty-two days, a delicate membrane at fifty-three days and a thick capsule at eighty-three days. Kaplan,[14] on the other hand, stated that it takes six weeks for formation of a capsule from the time of development of symptoms.

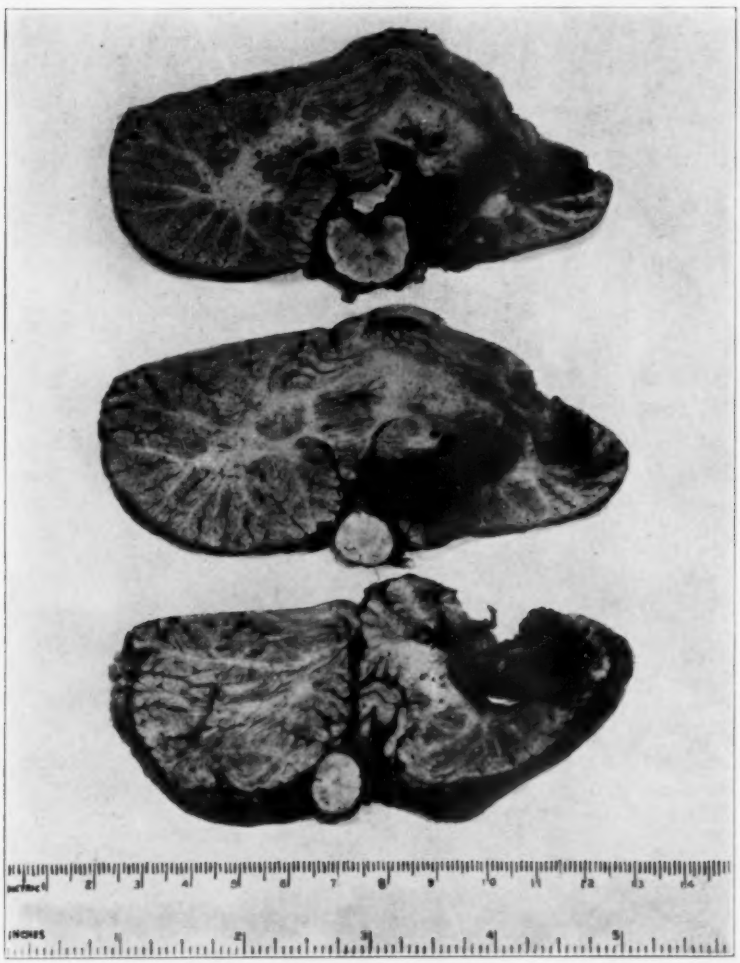

Fig. 5.—A cerebellar abscess of three weeks' duration, secondary to mastoid disease and caused by Str. haemolyticus. Despite the gross appearance, the abscess has a good capsule.

13. Huguenin, G.: Encephalitis und Hirnabszess, in von Ziemssen, H.: Handbuch der speziellen pathologie und Therapie, Leipzig, F. C. W. Vogel, 1876, vol. 2, p. 331.

14. Kaplan, A.: Abscess of the Brain, Arch. Otolaryng. **21**:385 (April) 1935.

In the present series no capsule formation was observed after three days in 1 case, but a beginning capsule was seen in a case of abscess of six days' duration. On the other hand, no capsule was seen in another case of abscess of ten days' duration, but a good capsule was present in a case of abscess of fourteen days' duration. At twenty-one days the capsule was forming well in 3 cases.

It seems evident from the experience of others as well as from the cases studied here that the optimum time for the formation of the capsule of an abscess is variable and cannot be stated definitely in every instance. There is no rule of thumb, therefore, which one may use in arriving at this decision. As Macewen [15] said:

> The time required for the formation of the abscess capsule is indefinite, and depends on the condition of the part and the character of the inflammation. Some abscesses of at least 3 weeks' duration were found to be without capsules.

This leads to consideration of the next problem in capsule formation:

Relation of Time to the Type of Capsule.—There is little doubt that time is an important factor in the development of the capsule of an abscess. This was emphasized by Globus and Horn and has been recognized by other investigators. It was true in a general sense in the cases I investigated. That it is not the only element cannot be emphasized too strongly. Due consideration must be given to the invading organism and the response of the host.

Generally speaking, the older the abscess, the greater the likelihood of encapsulation. A review of the cases shows that in the group of early abscesses there was no capsule at three days, a beginning capsule at six days, again no capsule at ten days and definitely greater evidence of capsule formation after from fourteen to twenty-one days. Abscesses of from three to six weeks' duration showed a good capsule in every instance. Abscesses of more than six weeks' duration showed variable results. One abscess, of two months' duration, had a poorly formed capsule, and another, of two and one-half months' duration, no capsule whatever. Still another abscess, of eleven months' duration, had poor encapsulation. On the other hand, 11 other abscesses, which varied in duration from two to eleven months, showed good encapsulation. It may be interesting to point out incidentally that the encapsulation of traumatic abscesses was always complete and was usually heavy.

The conclusions to be drawn from this experience are: 1. In general, the older the abscess in the brain, the greater the likelihood of encapsulation. It does not follow from this, however, that every abscess as it becomes older and more chronic becomes more heavily, or

15. Macewen, W.: Pyogenic Infective Diseases of the Brain and Spinal Cord, Meningitis, Abscess of Brain, Infective Sinus Thrombosis, Glasgow, J. Maclehose & Sons, 1893.

even adequately, encapsulated. Exceptions to this rule have been cited from my own experience and that of other authors. The occurrence of an abscess of eleven months' duration in which there was no question of cerebral infection during the entire period and which had no capsule makes it possible to say only that in most cases a capsule will develop

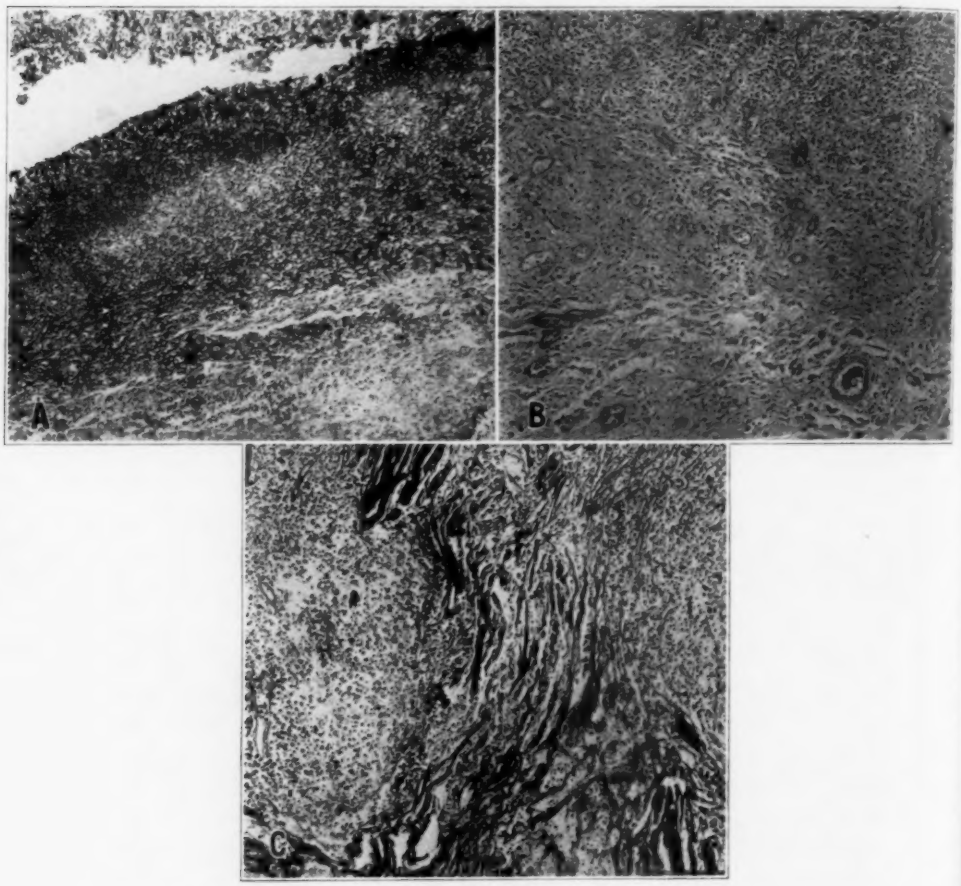

Fig. 6.—An abscess of three weeks' duration. With the hematoxylin-eosin preparation (*A*) little fibrous tissue is seen, but with the Masson trichrome stain (*B*) a heavy fibrous carpet is visible. The participation of the dura in the formation of the capsule in this case is clearly seen in *C*, in which the heavy strands of fibrous tissue represent prolongations of fibrous tissue from the dura. The causative organism was Streptococcus subacidus haemolyticus.

in time. 2. It does not follow, furthermore, that as an abscess becomes older the capsule becomes heavier. On the other hand, Cairns and

Donald [16] expressed the belief that abscesses of long duration usually have thick walls, whereas acute abscesses are not thick walled. The present study and the experience of other authors indicate clearly that abscesses of short duration (twenty-one days) may be heavily encapsulated, while older abscesses may possess inadequate capsules. The reason for this fact is not clear. It is obvious, however, that in cases of traumatic abscess a heavy capsule is almost always present because of the participation of the dura and the pia mater in the formation of the capsule. The density of the capsule is dependent also on the bacterial population of the abscess, just as its presence is. The clinical significance of these factors will be considered subsequently.

Relation of the Causative Organism to the Formation of the Capsule.—It has been suspected for some time that there is a close correlation between the organisms found in the capsules of abscesses and the subsequent histologic structure of the capsule. Efforts have been made from time to time to relate specific features of abscess formation to the bacteriologic content of the abscess.

Type of Bacteria: There have been many studies of the various types of bacteria found in abscesses of the brain. Evans [17] found that in infections of the middle ear and mastoid multiple organisms, staphylococci, streptococci and pneumococci were usually present; in abscesses from intrathoracic suppuration the streptococcus was usually grown in pure culture, and in multiple abscesses due to general pyemia the staphylococcus was usually the only organism found. Of 28 cases of abscess of the brain Coleman [18] found the condition due to the staphylococcus in 13, to the nonhemolytic streptococcus in 5, to the streptococcus in 3, to the enterococcus in 1 and to organisms of undetermined type in the rest. Dolger [19] found the streptococcus most commonly present in otogenic abscess of the brain. Bacillus proteus, Bacillus coli and Bacillus pyocyaneus also were found, but not as commonly as the streptococcus. He stated that most authors regard the streptococcus as the most common organism in abscess of the brain. On the other hand, Forselles [20] found that in 29 cases the following bacteria were obtained: Pneumococcus in 14, B. coli in 12, Streptococcus in 5, Staphylococcus in 4, and other organisms in 3. There were negative cultures in 3. Homen

16. Cairns, H., and Donald, C.: The Diagnosis and Treatment of Abscess of the Brain, J. Laryng. & Otol. **50**:73 (Feb.) 1935.

17. Evans, W.: The Pathology and Etiology of Brain Abscess, Lancet **1**:1231 (June 6); 1289 (June 13) 1931.

18. Coleman, C. E.: Brain Abscess, J. A. M. A. **95**:568 (Aug. 23) 1930.

19. Dolger, H.: Zur Bakteriologie der otogenen endokraniellen Komplikationen, Zentralbl. f. Hals-, Nasen- u. Ohrenh. **11**:49, 1927-1928.

20. af Forselles, A.: Der otitische Hirnabszess: Pathologie und Therapie, Acta oto-laryng. **10**:395, 1927.

found the streptococcus, the staphylococcus, the pneumococcus, Corynebacterium pseudodiphthericum, B. pyocyaneus and B. coli in a number of cases of abscess of the brain. Haszlauer [21] made an extensive study of the bacteriologic content of abscesses of the brain. It is impossible to quote his findings in extenso. Briefly stated, they are as follows: Of 11 cases of acute abscess of the brain he found the streptococcus in 6 and various combinations of staphylococci, streptococci and diplococci in the others; of 34 cases of chronic abscess the streptococcus was cultured in 10, with the diplococcus, the staphylococcus, B. pyocyaneus, Bacillus typhosus and Bacillus tuberculosis in the others; of 16

Fig. 7.—A cerebellar abscess of three weeks' duration caused by the pneumococcus and secondary to otitis media. The capsule is well formed.

other cases the streptococcus was found in 5 and various other bacteria in varying combinations in 11. Of 61 cases of abscess of the brain, therefore, Haszlauer found the streptococcus in 27, in 22 of which it was found in pure culture. Homen expressed agreement with this observation; he stated that the streptococcus is the most frequent cause of abscess of the brain and the staphylococcus the next most common bacterial agent. Macewen also found the streptococcus most frequently in his cases of abscess of the brain. On the other hand, Piquet and

21. Haszlauer: Die Mikroorganismen bei den endokraniellen otogenen Komplikationen, Internat. Zentralbl. f. Ohrenh. **5**:1, 1907.

Minne [22] found the streptococcus in only 3 of 16 cases of cerebral abscess and in only 1 of 6 cases of cerebellar abscess; the pneumococcus, the staphylococcus and B. proteus were found almost as frequently as the streptococcus.

Among my 27 cases of abscess of the brain the causative organism was distributed as follows:

	Cases
Staphylococcus aureus	4
Staphylococcus aureus haemolyticus	7
Streptococcus haemolyticus	5
Pneumococcus	5
Staphylococcus albus haemolyticus	3
Streptococcus subacidus	1
Gram-negative rod	1
Streptococcus subacidus haemolyticus	1

The staphylococcus outnumbered the streptococcus by far. No correlation could be made between the focus of infection and the type of organism found in the abscess. Thus, staphylococci or streptococci occurred as frequently in sinal infections as in infections of the mastoid or the middle ear.

Bacteria and Capsule Formation: While it is desirable to know what sort of bacteria inhabit abscesses of the brain, it is even more important to know the relation of the various forms of organisms to the formation of the capsule of the abscess. Some steps have been made in this direction. Brunner [23] stated that it is well known that destructive and necrotic changes are enhanced by the gram-negative anaerobic bacteria, while the aerobic bacteria influence the reparative process and hence capsule formation. Neumann,[24] who was among the first to correlate these findings, stated that the anaerobic bacteria prevent the formation of capsules, while the cocci, especially the capsular cocci, produce a layer of fibrin soon after penetration into the substance of the brain and hence lead to the formation of a capsule. Linck [25] found that the diplococci and staphylococci enhance the formation of a capsule, while gram-negative rods in conjunction with cocci prevent the formation of a membrane. Homen found that in cases in which anaerobic and aerobic bacteria were present together the proliferative processes were slight or were not present at all.

22. Piquet, J., and Minne, J.: Considerations sur les abcès encéphaliques, Ann. d'oto-laryng., October 1936, p. 993.

23. Brunner, H.: Otogene endokranielle Erkrankungen, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 10, p. 194.

24. Neumann, H.: Otitic Cerebellar Abscess, London, H. K. Lewis, 1909.

25. Linck: Beitrag zur Klinik und Pathologie der Hirnabszesse, Deutsche Ztschr. f. Chir. **166**:65, 1921.

It seems to be agreed that anaerobic bacteria do not favor the formation of a capsule, while aerobic bacteria, especially the cocci, favor capsulation.

More important still is the question of possible direct correlation between the type of organism and the formation of a capsule. For the abscesses in which capsule formation was inadequate or absent the results of bacteriologic study are shown in the following tabulation:

Duration of Abscess	Focus	Organism
10 days	Sinuses	Staph. albus nonhaemolyticus
2 mo.	Sinuses	Pneumococcus and streptococcus
2½ mo.	Sinuses	Gram-negative rod and Achromobacter
4 mo.	Sinuses	Staph. aureus nonhaemolyticus
11 mo.	Sinuses	Staph. albus haemolyticus

The only observation to be drawn from this group of cases is that the staphylococcus is prone to form a poor capsule under certain conditions. This should not be relied on absolutely, because the experience of other authors has shown definitely that the staphylococcus is usually a good capsule-forming organism. Ramadier, Caussé, André-Thomas, Barré and Velter [26] found that cocci tend to produce an encapsulated abscess, while bacilli, especially the anaerobic group, cause encephalitis with no capsule formation. No inferences can be drawn from the fact that in all the cases the primary focus was in the sinuses. Among well encapsulated abscesses the staphylococcus, streptococcus and pneumococcus seemed equally capable of forming capsules.

In a consideration of the role of the invading organism in the production of abscess, in addition to the type of organism and the resistance of the host, great importance must be attached to the virulence of the organism, the presence or absence of an infection of the blood stream and the state of activity of the primary focus. The relation of the virulence of the organism to the form of the capsule has been well recognized by Courville and Nielsen,[27] who found that in the acute abscesses with poor encapsulation a virulent organism was at work, while in the heavily encapsulated abscesses a more chronic avirulent organism was at work. Homen too found that the older the process, the more marked are the proliferative and reparatory changes, owing in part to a decrease in the virulence of the bacteria and to destruction of the invading organisms. It is clear that a virulent organism in the blood stream will cause death before an adequate capsule can be formed, even though the beginnings of an abscess are present. Further-

26. Ramadier, J.; Caussé, R.; André-Thomas; Barré, J. A., and Velter, E.: Les abcés du cervelet, Rev. d'oto-neuro-opht. **13**:1 (Jan.); 85 (Feb.) 1935.

27. Courville, C. B., and Nielsen, J. M.: Otogenous Abscess of the Parietal Lobe, Arch. Surg. **30**:930 (June) 1935.

more, an active, patent focus of infection in the sinuses or mastoid may so lower the resistance of the patient as to make the possibility of abscess formation definitely less than in chronic, less virulent foci. It is well known that abscess of the brain is more frequently a complication of chronic than of acute otitis media or mastoiditis.

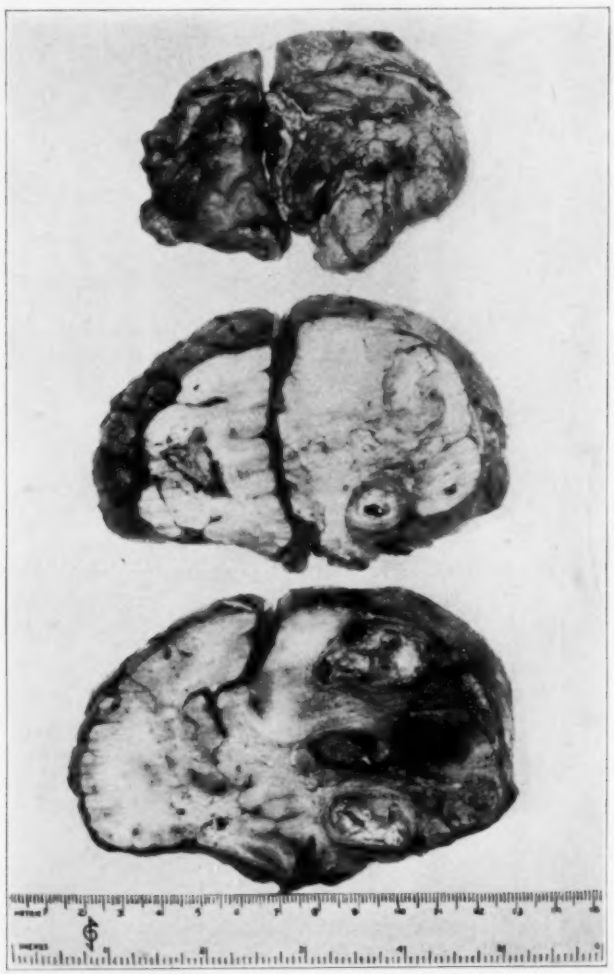

Fig. 8.—A well encapsulated abscess of six weeks' duration due to Staph. aureus and secondary to disease of the frontal sinus.

Much remains to be clarified, then, concerning the relation of bacteria to the formation of encapsulated abscesses, but this much seems clear: Anaerobic bacteria are poor capsule formers; conversely, aerobic bacteria form good capsules; mixed infections are on the whole not conducive to good capsule development. It would be well to know

how to measure the virulence of the invading organism and the resistance of the host in determining whether a capsule has been or will be formed.

Histologic Structure of the Capsule.—Time and the type of organism are important in the formation of the capsule of an abscess. The next problem which arises is the exact nature of the capsule.

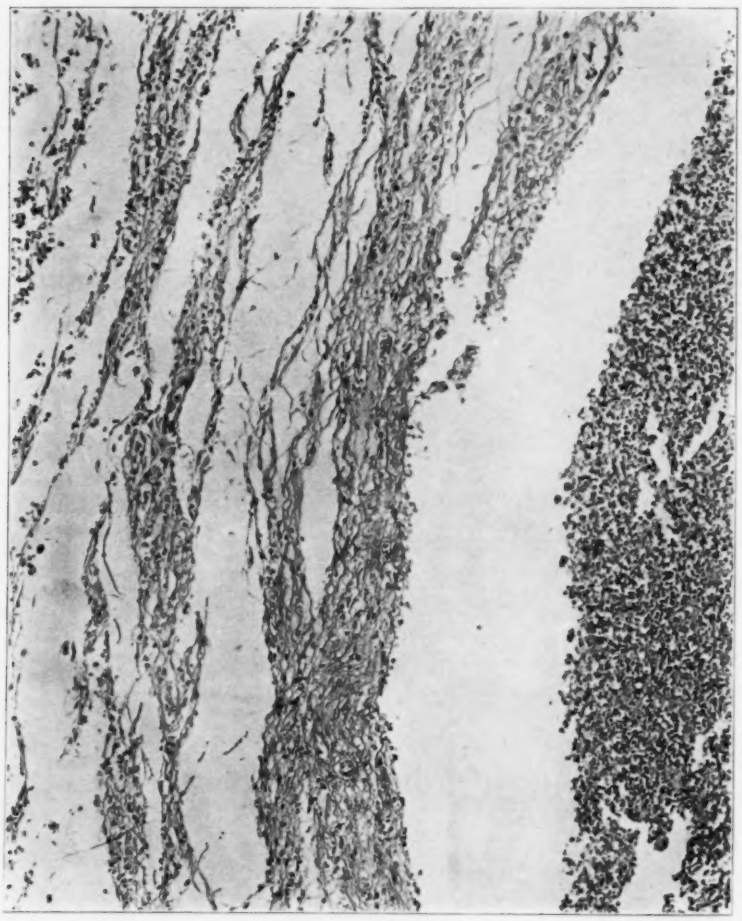

Fig. 9.—An abscess of two months' duration (hematoxylin-eosin stain). The fibrous wall of the capsule is clearly evident. This was a mixed pneumococcic-streptococcic infection.

Collagenous Structure of the Capsule: It is generally agreed that practically always the capsule of an abscess is composed entirely of elements of connective tissue. The participation of neuroglia in the formation of the capsule is either insignificant or totally lacking. In none of my 26 cases was there any evidence of active participation of

neuroglial elements in the formation of the capsule itself. Neither Holzer nor silver stains revealed the formation of a neuroglial net as

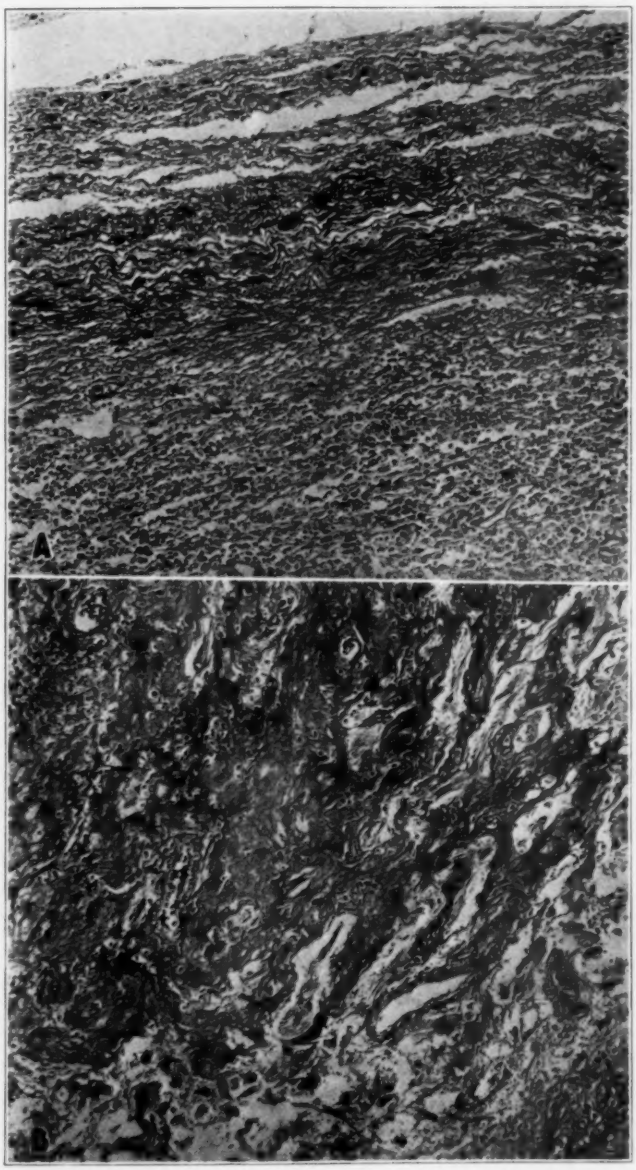

Fig. 10.—An abscess of three months' duration. The development of a heavy capsule is evident. The organism was Staph. aureus.

part of the capsule. Even in the surrounding brain tissue no evidence of gliosis was observed around the abscess except late in the develop-

ment of the wall of the abscess. This gliosis occurred in the surrounding brain tissue and could not be regarded as part of the wall of the abscess proper. Even so, it was present in only a few instances and could not be regarded as a common feature of the process of encapsulation.

Fig. 11.—Multiple abscesses of four months' duration in the frontal lobe, secondary to disease of the ethmoid sinus and due to infection by Staph. aureus. The capsule is heavy and well formed.

Other investigators, on the other hand, have seen evidence of glial participation in the capsule formation. Globus and Horn noted that, as the collagenous fibers increased in amount, glial proliferation contributed its share toward the strengthening of the limiting wall about

the suppurative process. Bagley [28] observed some capsules formed almost entirely of neuroglial fibrils. Such capsules are usually thin, because of the delicate nature of the neuroglial fibrils. Nauwerk [29] described the capsule of an abscess composed entirely of neuroglia in a man aged 63 in whom an abscess of the left frontal lobe developed after a bullet wound. Knapp [30] saw 1 abscess among 19 in which the capsule was composed of neuroglial elements alone. This, too, followed a bullet wound in the head.

Despite these observations concerning the participation of the neuroglia in the formation of the capsule of the abscess the present group of cases does not support this point of view. Other authors have noted abscess capsules formed exclusively of collagenous tissue. Westphal, who made a careful study of abscesses of the brain, observed that the capsule was formed chiefly of connective tissue and that the glial reaction was in the surrounding brain tissue near the capsule but not actually a part of it. Midowski also noted that the capsule was entirely made up of elements of connective tissue. Hassin [31] saw only participation of the elements of connective tissue. Kölpin [32] observed no evidence of neuroglial participation in the capsule formation.

Origin of the Capsule.—The fibrous or connective tissue capsule takes its origin from various sources. It is derived from (1) the blood vessels, (2) lymphocytes and (3) the dura and pia mater in cases of trauma.

Most of the collagen is probably derived from fibroblasts which take their origin from the many small blood vessels in the reactive zone of the abscess. This derivation can be seen readily even with routine stains. This was certainly true in my cases of abscess and has been observed by Kölpin, who saw fibroblasts coming from the walls of the blood vessels and depositing collagen to form the capsule. Similarly, Midowski noted that the collagen was derived from the blood vessels. Neumann expressed the opinion that not only the blood vessels but the fixed elements of connective tissue gave origin to the fibrous capsule. Since in the brain these fixed elements are in the wall of the vessel and in the pial prolongations around the vessels, they can be regarded

28. Bagley, C., Jr.: Brain Abscess with Pathological Observations, Surg., Gynec. & Obst. **38**:1 (Jan.) 1924.

29. Nauwerk, C.: Beiträge zur Pathologie des Gehirns, Deutsches Arch. f. klin. Med. **29**:1, 1881.

30. Knapp, E.: Zur Pathogenese der bindegewebigen und gliösen Abkapselung von Hirnabscessen, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:44, 1932.

31. Hassin, G. B.: Histopathology of Brain Abscess, with Remarks on Intraspinal Therapy, Arch. Neurol. & Psychiat. **3**:616 (June) 1920.

32. Kölpin: Zur Symptomatologie und pathologischen Anatomie des Hirnabszesses, Deutsche Ztschr. f. Nervenh. **25**:465, 1904.

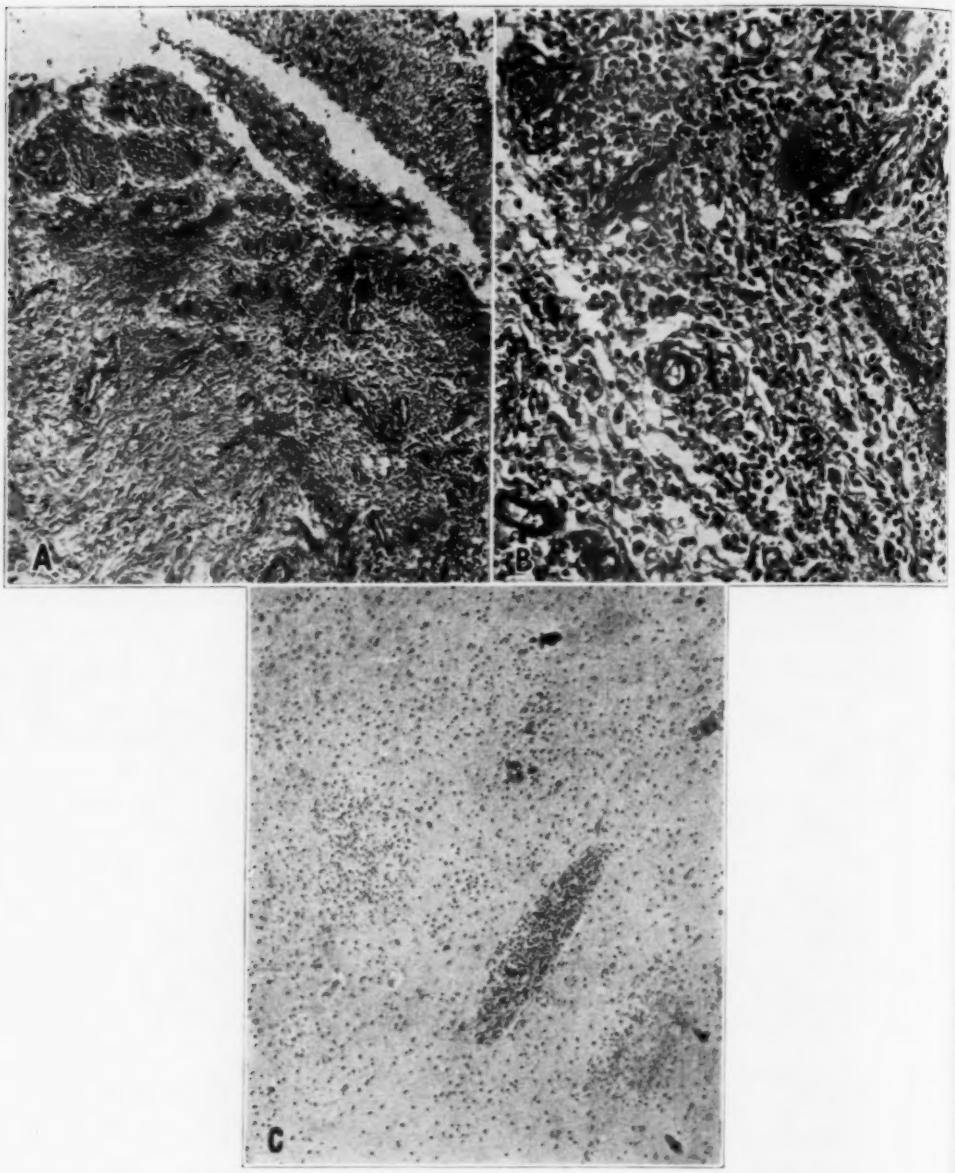

Fig. 12.—This abscess is of long standing (eleven months), yet the capsule formation is incomplete. The hematoxylin-eosin stain (*A*) shows the formation of some connective tissue in the wall of the abscess adjacent to the cavity. This is seen in *B* to be a diffuse reticular deposit. In *C* is seen the encephalitis in the adjacent brain tissue. The causative organism was Staph. albus haemolyticus.

essentially as originating from blood vessels. Westphal stated the belief that the capsule was formed chiefly from elements of connective tissue derived from the pia, but this point of view has not been substantiated either by my studies or by those of other authors, except in cases of abscess secondary to cranial trauma.

Some of the fibroblasts and collagen tissue which make up the fibrous capsule appear to be derived from lymphocytes which become converted into fibroblasts. Hassin stated that the collagen is derived exclusively from the lymphocytes, and a similar view was expressed by Globus and Horn.

In some instances the capsule is derived from the dura and pia. This is true in cases of traumatic abscess of the brain due to a penetrating wound of the skull. As a result of such a wound, a piece of dura and pia may be wedged into the cortex and become the nexus for the development of a stout fibrous capsule. In my cases of ordinary abscess of the brain, however, I have found no evidence that the pia or the dura participates in the formation of the capsule of the abscess.

CLINICAL CORRELATIONS

Many of the points of clinical importance have already been mentioned in my discussion of the histologic features of abscess formation. They may bear recapitulation, however, for the sake of emphasis. It has been stated that time is the most important element in the formation of the capsule of an abscess. Hence it seems reasonable to assume that in cases of acute abscess the longer one waits before operation the better is the chance of encountering a walled-off abscess. This is true in most cases, but there are well known instances in which no encapsulation or inadequate encapsulation has occurred after several months. In most cases, if the situation is not too acute, it seems advisable to wait at least three weeks and preferably four for encapsulation and hence operation. This is not always possible, because in some cases the onset is so acute and the situation so desperate that immediate intervention seems necessary. It is doubtful whether operation would do more than satisfy anxious relatives in such cases, because, histologically, only encephalitis is present; the abscess has not yet formed. On the other hand, that this is not invariably the case is shown by an occasional recovery from a very acute condition after operation before encapsulation has occurred.[22] When such an acute condition is present it is probably better first to remove the focus of infection in the sinuses or mastoids and to follow the removal by a period of watchful waiting, in the hope that the type of organism and the resistance of the patient will permit encapsulation.

It is desirable to point out also that an encapsulated abscess is not by any means a quiescent abscess. Within the cavity of the abscess may be virulent bacteria, which if permitted to escape into the meninges may produce fatal meningitis. Practically all abscesses contain bacteria. Only occasionally is a sterile abscess encountered.

This fact is intimately associated with the problem of encephalitis around some of the abscesses. Even in the case of old abscesses one sometimes finds active encephalitis in the tissue around the capsule. In my series this encephalitis was invariably a sign of an active abscess. It would seem desirable to know whether such encephalitis is present in certain cases in order to be prepared for it in the operative approach. Thus far, however, no signs have been found which could be regarded as characteristic of this encephalitic reaction.

CONCLUSIONS

1. Twenty-seven abscesses of the brain have been studied histologically and bacteriologically.

2. Their histologic structure is described, especially with reference to the formation of the capsule of the abscess.

3. Time, the type of organism and the resistance of the host are the most important factors in the development of the capsule.

4. The optimum time for capsule formation is three to four weeks.

DIFFERENTIAL DIAGNOSIS OF INTRINSIC CARCINOMA OF THE LARYNX

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The suggestion that this paper should be presented emphasizes the difficulties encountered even by the most careful observers. Not only is there a danger that treatment, by operation or otherwise, may be instituted under a mistaken diagnosis of malignant disease, but there is another and even greater danger, that malignant change may be overlooked until the disease has progressed beyond the chance of cure.

It is desirable, therefore, to review the possible mistakes of omission and commission and to consider the means of avoiding them.

COMMON SOURCES OF CONFUSION

The diseases which most commonly cause confusion are: (*a*) chronic diffuse simple laryngitis; (*b*) hypertrophic laryngitis, hyperkeratosis and pachyderma; (*c*) syphilitic infiltration and leukoplakia; (*d*) tuberculous laryngitis, and (*e*) simple neoplasm. Any one of these conditions may simulate carcinoma so closely as to lead to the adoption of such drastic treatment as laryngectomy. On the other hand, a mistaken diagnosis of any one of the less virulent diseases may be made while all the time unrecognized malignant cells are invading the surrounding tissues.

I propose to limit the discussion to intrinsic carcinoma of the larynx, as a growth on the aryepiglottic folds, the epiglottis or the posterior surface of the larynx rarely offers much difficulty in diagnosis.

(a) *Chronic Diffuse Simple Laryngitis.*—A patient may complain of long-standing or progressive hoarseness, and the signs may be those of chronic inflammation. The whole larynx may be inflamed, and the arytenoepiglottic folds—if involved in the process—may appear thickened and infiltrated (fig. 1). The vocal cords will have lost their luster and the margins appear rounded and thickened. If on one cord, particularly at its anterior region, the mucosa is seen to be of irregular thickness, considerable doubt may arise as to whether malignant change has commenced.

In such cases there may be nasal obstruction or chronic inflammatory change in the nose, the sinuses, the mouth or the pharynx; these must

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be sought for and treated. The use of tobacco or alcohol and misuse of the voice may be contributory factors.

In an elderly man—and it is, of course, here that doubt arises—it is unlikely that simple deviation of the septum or chronic sinusitis will be sufficient to produce increasing hoarseness; the presence of either is

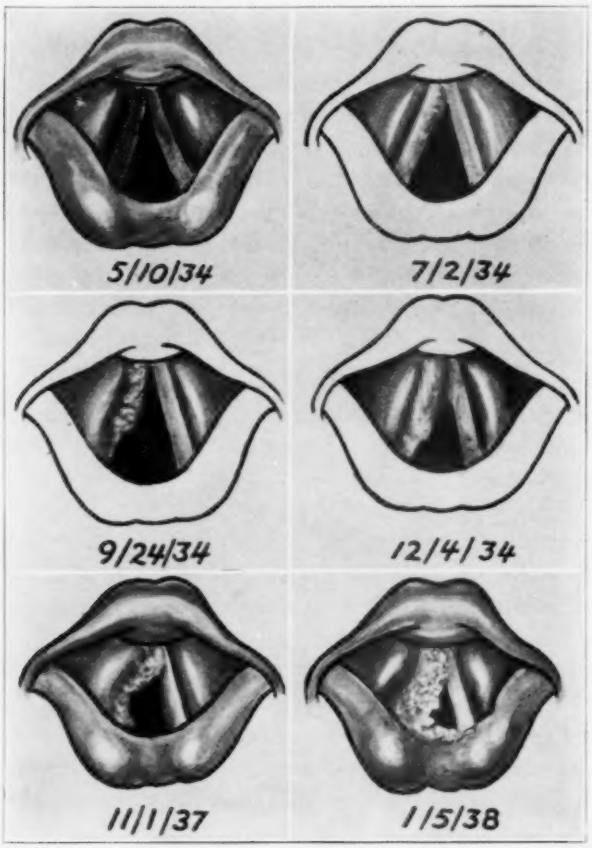

Fig. 1.—Carcinoma of the larynx, associated with chronic laryngitis. The patient, a man of 67, suffered from hoarseness of some years' duration. This symptom had recently become more pronounced. There was diffuse laryngitis with inflammation of the vocal cords and swelling of the arytenoepiglottic folds. Examination was difficult, but at the anterior end of the right cord a suspicious thickened area was noticed on May 10, 1934. Vocal rest and suitable treatment of the laryngitis and associated pharyngitis brought a definite carcinoma to view on July 2. The affected cord was removed and the anterior end of the opposite cord, which was rough and suspicious, was coagulated by diathermy. Granulations formed in the operative area on September 24, with subsequent (December 4) contraction and narrowing of the glottis. Chronic inflammatory changes had recurred on Nov. 1, 1937, and by Jan. 1, 1938, hyperkeratosis and signs suggestive of malignant change were present. Treatment with teleradium arrested the disease and improved both the airway and the voice.

no new strain on the man, who will probably have become habituated to partial or complete mouth breathing.

Infected tonsils are a cause of worry, because advising their removal for diagnosis is somewhat drastic; probably simple treatment with a weak iodine paint or the use of one of the silver compounds as a spray or for swabbing will be sufficient to produce improvement.

A reasonable interval must be allowed to elapse after the commencement of treatment before malignant change can be excluded; even if a growth is eventually found, much will have been gained and nothing lost by preliminary treatment to improve the condition of the upper air and food passages.

Smoking should be abandoned; the use of alcohol must be kept within limits, and the use of the voice must be reduced or, preferably, avoided altogether. Silence for three weeks will clear up the condition in some cases and in others will define a growth. The diffuse inflammation of the larynx should have subsided; the pharynx should be less sensitive and examination easier. It may then be possible to see a localized projection from the vocal cord, with a definite appearance of carcinoma (fig. 1).

The localization of the outgrowth on the anterior segment of one cord will strongly support a suspicion of malignant growth. Intrinsic cancer rarely starts elsewhere and is almost unknown at the posterior extremity of the cord or in the interarytenoid region.

If a definite neoplasm is visible, it may be desirable to remove a piece, not only to confirm the diagnosis of malignancy but to determine the type of growth, with a view to deciding on suitable treatment.

The suspicion that a subglottic growth is present may require more prolonged investigation or possibly direct examination with a laryngoscope.

(b) *Hypertrophic Laryngitis, Hyperkeratosis and Pachyderma.*—This may occur as diffuse infiltration of the vocal cords and ventricular bands; there may be a localized tuberosity over the vocal process, known as pachyderma laryngis, or a heaping-up in the interarytenoid region, and, finally, an isolated plaque of keratosis may be present, particularly on the anterior third of one vocal cord. Localized or diffuse overproduction of the superficial epithelium offers considerable difficulty in deciding whether malignant changes are commencing in the deeper layers of what is a potentially precancerous condition. A progressive change in appearance or an increase of symptoms gives warning that a simple process—possibly present for years—is changing its character. Biopsy may be required to settle the question as to whether drastic treatment is required. Localized deposits over the vocal proc-

esses or at the posterior end of the glottis should not be mistaken for carcinoma, because, as Sir St. Clair Thomson has repeatedly emphasized, malignant growth rarely, if ever, originates in this region. Furthermore, such hypertrophy may be recognized by its response to treatment. The most usual manifestation of keratosis is a patch on the anterior third of a vocal cord. This may be flat and isolated, but it may possibly be associated with an area of malignant infiltration. Biopsy may make possible a positive diagnosis of carcinoma, but not always.

Two alternatives present themselves: one to wait and see and the other to remove the infiltrated area—if localized—by laryngofissure or with radium, according to individual circumstances. When the surgeon is in doubt, the wiser course is to adopt active treatment.

(*c*) *Syphilitic Infiltration and Leukoplakia.*—Syphilitic disease of the larynx is nowadays such a rarity, at least in the southern part of England, that its exclusion is probable in practically all cases. Occasion-

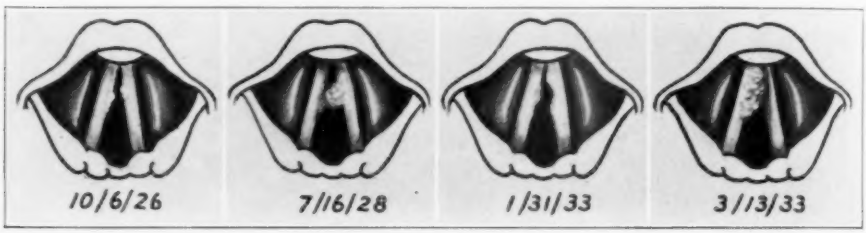

Fig. 2.—Syphilitic leukoplakia with subsequent malignant change. On Oct. 6, 1926, whitish irregular infiltration was present in the vocal cords; mercury and neoarsphenamine were administered. On July 16, 1928, a piece removed for biopsy showed granuloma with keratosis. Another biopsy on Feb. 21, 1930, showed the same picture. There was no evidence of malignancy. Potassium iodide was given. Biopsy on March 13, 1933, showed carcinoma, group 1. Operation or interstitial application of radium was refused. The patient was referred for teleradium treatment, which was given after removal of ossified portions of the thyroid cartilage. Stenosis followed, and later bronchopneumonia occurred. (The case was observed in association with Sir St. Clair Thomson.)

ally a patient with hyperkeratosis of long standing, presumably associated with syphilis, may be seen (fig. 2). The results of antisyphilitic treatment, however drastic, are disappointing, and the condition may drift on until malignant change appears and calls for the appropriate treatment. An aid to diagnosis is the observation that syphilitic foci are multiple and thus differ from malignant neoplasms, which are single; also, syphilis usually affects the pharynx as well as the larynx.

(d) *Tuberculous Laryngitis.*—In tuberculosis lies a great danger, not only of submitting patients to an unnecessary operation under a mistaken diagnosis of carcinoma but of neglecting to recognize and

deal actively with a malignant growth because the patient is suspected of having tuberculosis. Patients have been seen by me on more than one occasion when all preparations for laryngofissure or total laryngectomy had been made although the correct diagnosis was tuberculous infiltration and not malignant growth (figs. 3 and 4).

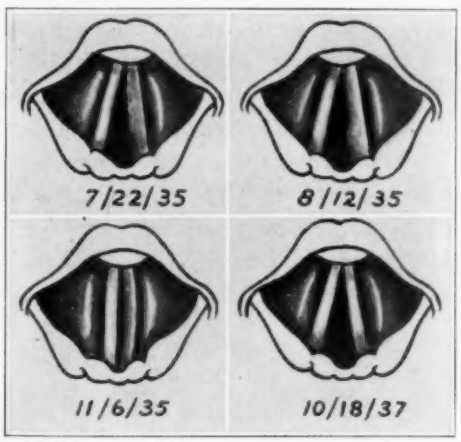

Fig. 3.—Tuberculosis wrongly diagnosed as carcinoma. On July 22, 1935, the patient came under observation, with a diagnosis of carcinoma of the larynx. There appeared to be infiltration of the left cord, mainly at the posterior end, with ulceration over the vocal process of the arytenoid. Movements of the cord were restricted. Widespread foci of tuberculosis were seen in the lungs roentgenographically. On August 12 some improvement was evident. On November 6 the patient had gained 8 pounds (3.6 Kg.). There was no ulceration of the vocal cord, but diffuse injection and some bowing were present. Later movements became perfect, and infiltration of the cord disappeared.

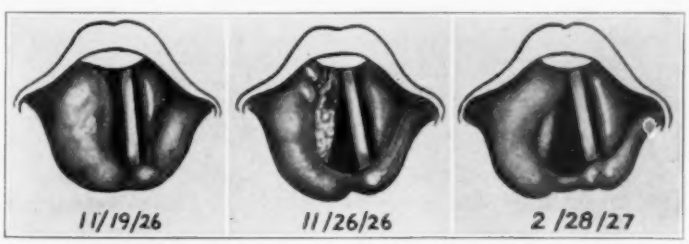

Fig. 4.—Tuberculosis of the larynx wrongly diagnosed as carcinoma. The patient, a man aged 44, was sent to me because of "carcinoma of the larynx" and was said to require laryngectomy. The right arytenoepiglottic fold was swollen and obscured the right cord, which was infiltrated and had an irregular margin. Direct examination showed the condition clearly; biopsy revealed chronic inflammatory changes, with giant cells. Roentgenograms showed deposits in the lungs; there was no history of tuberculosis. Under treatment in a sanatorium the condition improved. The patient eventually recovered his health and voice and returned to his occupation as a cattle rancher in South America.

Tuberculosis may show itself as diffuse and irregular thickening of the whole of one cord, even with fixation, but usually there is suspicious ulceration over the vocal process or in its neighborhood. On the other hand, the patient may have an indolent type of infiltration. If he is below the usual age for malignant laryngeal growth, the suspicion of tubercle should be aroused. There may be associated pseudoedematous swelling of the aryepiglottic fold. Both the history and the results of physical examination may give no suggestion that the lungs are affected, but roentgen examination should show deposits if any are present.

In a woman appearances suggestive of malignant growth are counterbalanced by the fact that women are seldom affected, but too much stress must not be placed on the improbability that carcinoma is present. Careful examination, always supported by roentgen examination, is necessary to establish a diagnosis, and in cases of doubt biopsy will be required.

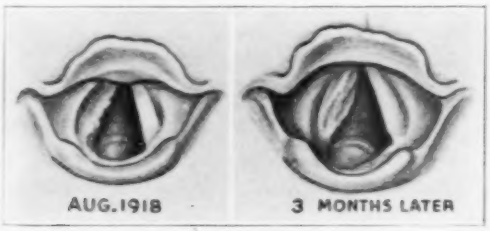

Fig. 5.—Carcinoma of the larynx mistaken for tuberculosis. The patient, a man of 53, was under the care of Sir St. Clair Thomson, who has lent the illustrations. The right cord appeared "mousenibbled" at the first examination. Three months later there was deeper infiltration, with the early white points of fungation of the growth and commencing dimpling. There was impairment of movement of the cord in abduction.

An opposite condition is sometimes, but rarely, encountered: A suspicion of tuberculosis may arise in a case in which the correct diagnosis is carcinoma (fig. 5). The absence of physical or roentgen signs in the chest, the steadiness of the temperature and the maintenance of weight are all factors of importance. Here again biopsy may be required.

Finally, there are cases in which hoarseness develops in a patient with recognized pulmonary tuberculosis. The first and natural conclusion is that the symptom is due to tuberculosis in the larynx. The general and local condition, the roentgen picture of the lungs, the temperature and the weight may all point toward this conclusion. However, atypical distribution of the laryngeal condition, on the anterior rather than the posterior parts of the vocal cords, may arouse a suspicion of carcinoma, and biopsy may be required (fig. 6).

Fig. 6.—Carcinoma of the larynx in a patient with pulmonary tuberculosis. The patient had been in a sanatorium and had suffered from hemoptysis. The clinical appearance suggested carcinoma, and this diagnosis was confirmed by biopsy. Laryngofissure was done, with a temporarily good result. Local recurrence was noted two and a quarter years later and was treated with teleradium, with a good result. (The case was referred to me by Sir St. Clair Thomson.)

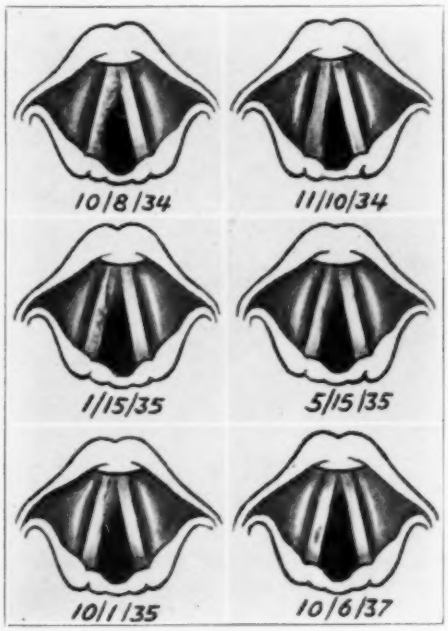

Fig. 7.—Intrinsic carcinoma of the larynx, treated by interstitial implantation of radium. The patient, a healthy man of 60, came to me on Oct. 8, 1934, with hoarseness of many months' duration. There was carcinomatous invasion along the whole length of the right cord. Radium needles were inserted on October 10, after removal of the greater part of the thyroid cartilage and part of the cricoid cartilage. The growth rapidly disappeared (compare views of Nov. 10, 1934, and Jan. 15, 1935), but anxiety was caused by a subglottic swelling at the anterior end of the glottis (observed on May 15 and Oct. 1, 1935). This was watched carefully, but it proved to be no more than the result of local perichondritis caused by the action of radium. It disappeared and left the larynx healthy as on Oct. 6, 1937. The patient had an excellent voice and a perfectly free airway at the time this report was made. (The case was referred to me by Sir St. Clair Thomson.)

It is, of course, necessary to be on guard against this possibility and thus to avoid the disaster of allowing a curable growth to become inoperable.

(e) *Simple Neoplasm.*—It is sometimes possible for a simple neoplasm to produce signs and symptoms suggestive of malignant disease. This may be true also of chondroma of the cricoid cartilage, which can appear sufficiently like subglottic carcinoma to require care in decision as to its nature.

If laryngoscopic examination with a mirror fails to establish a definite diagnosis, direct examination will be required; the hardness and smoothness of the tumor should then reveal its true nature.

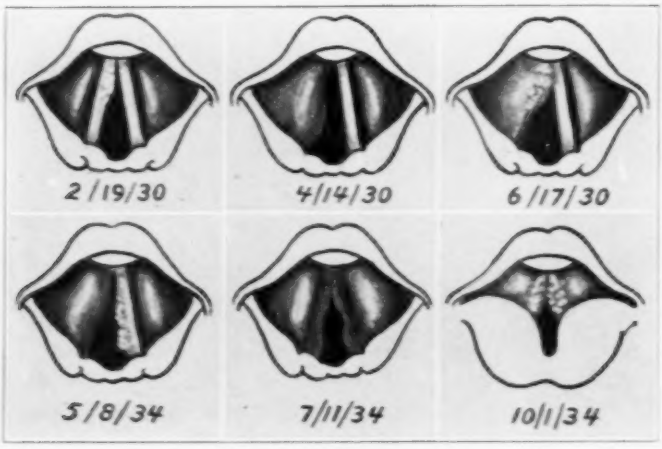

Fig. 8.—Intrinsic carcinoma of the larynx with recurrence. A man of 69 years had obvious localized carcinoma of Broder's group 1 when examined on Feb. 19, 1930. It was removed by laryngofissure on March 5, and examination on April 14 showed a good result. Granulations had appeared on June 17 but healing then took place, and all went well for four years. Recurrence was noticed on the opposite cord on May 8, 1934. The growth was removed on May 15. In three months the growth returned and necessitated total laryngectomy. Healing was satisfactory, but the patient soon died of emphysema and myocardial degeneration of the heart.

Simple papilloma in an adult may simulate malignant disease, but generally a suspicion of carcinoma must always be in the surgeon's mind in cases of such involvement, unless he can find definite evidence that it is not present.

SIMPLE GRANULATIONS

During the healing process after treatment of carcinoma of the larynx by operation or irradiation, a time may come when a fresh out-

growth appears, either at the anterior end of the excavation left by operation or near the anterior commissure after interstitial irradiation. No undue alarm need be felt, as the new formation is in all probability simple granuloma. I have watched, with Sir St. Clair Thomson, such a condition persisting for one year after the original growth had disappeared as a result of insertion of radium needles, but all abnormality

Fig. 9.—Simple granuloma of the larynx, with subsequent malignant changes. The patient, a woman, was a singer. On Jan. 3, 1918, she had a nodule on the left vocal cord. By Aug. 5, 1927, her voice was husky, and a semipedunculated outgrowth was present on the left cord. Biopsy showed a fibrous stroma with no sign of malignant change. The nodule was removed again on May 22, 1928. Examination on Nov. 18, 1929, showed keratosis. Vocal rest and local application of silver nitrate were prescribed. On July 3, 1930, a white projecting infiltration was present at the anterior end of the left cord. Biopsy showed hyperplastic epithelium with orderly cells, but no invasion. The appearance improved, and no operation was performed. Biopsy on March 18, 1931, was reported as showing "no sign of malignancy." By May 18 the growth was evident; radium needles were inserted by Mr. Colledge. The glands became involved by squamous cell carcinoma and were removed. On Jan. 5, 1932, the larynx appeared almost completely normal. Swelling of the left arytenoepiglottic fold, with enlargement of the glands, was evident on August 16. By March 8, 1933, growth was evident in the larynx, half of which was removed, with good recovery. Five months later the epiglottis showed deposits; further operation was followed by fatal pneumonia. (The case was observed in association with Sir. St. Clair Thomson.)

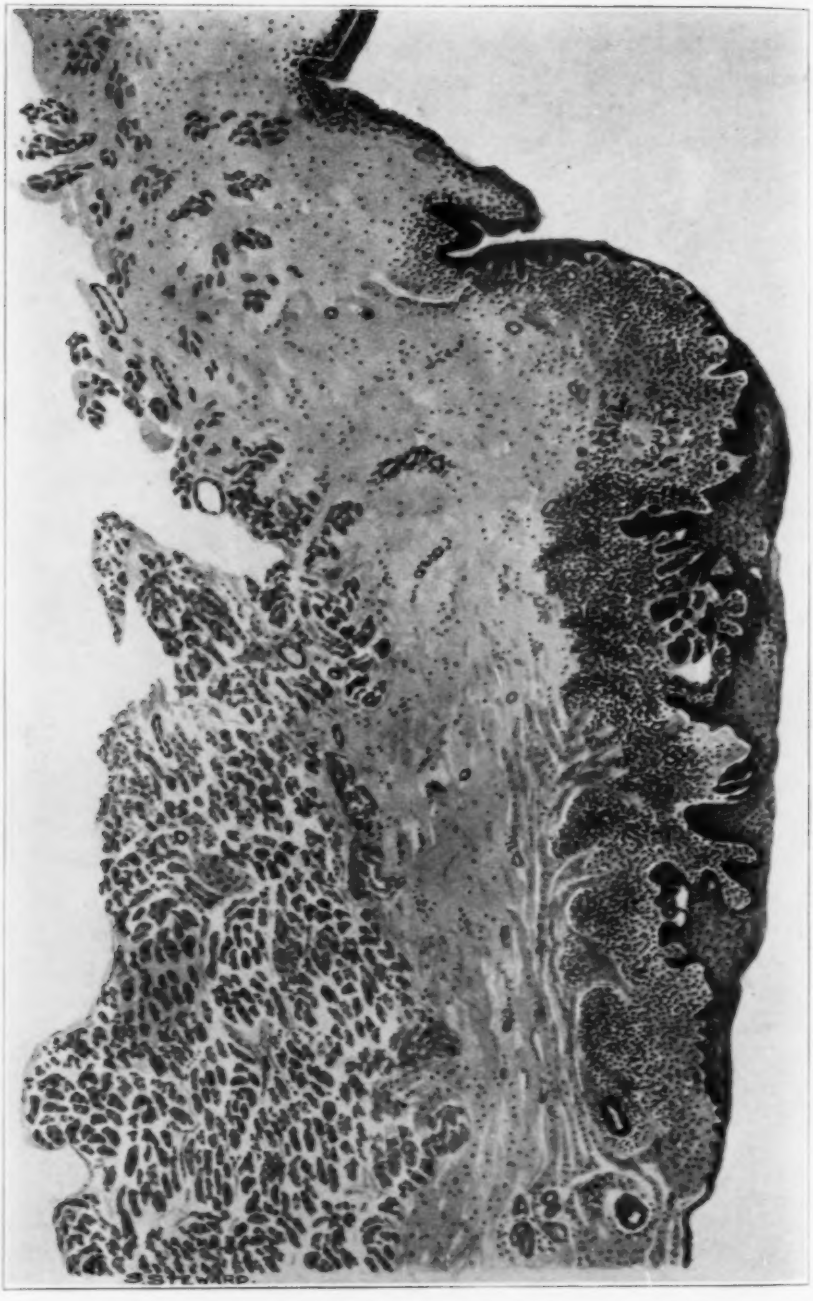

Fig. 10.—Section from carcinoma of the vocal cord. The patient, a man aged 46, had been hoarse for several months. A projecting growth was seen at the anterior end of the right vocal cord. The cord was removed by laryngofissure, with rapid recovery. The voice became strong and of good quality. In a limited area on the opposed surface of the cord the epithelium can be seen invading the deeper tissues in an irregular manner.

finally subsided, leaving only some scar tissue (fig. 7). The whole process was evidently the result of the formation of simple granulation tissue from slight localized chondritis. Such occurrences must be watched carefully, as in other cases they may not turn out so favorably (fig. 8).

MISLEADING RESULTS OF BIOPSY

Although the microscopic examination of a small piece of tissue may be of the greatest help in establishing a diagnosis of carcinoma or in determining the degree of malignancy, in certain cases only confusion may result. Some surgeons consider biopsy an undesirable proceeding, tending to cause spreading of malignant cells. However, even if this objection is overruled by experience to the contrary, there is still the danger that wrong conclusions may be drawn. In the sections nothing more than hypertrophy of the epithelium, with no sign of malignant invasion, may be seen simply because in removing a portion of tissue for microscopic examination the surgeon has not gone deep enough to embrace the cancerous area. If the clinical appearances strongly suggest carcinoma, less harm will be done by ignoring the pathologist's report and treating the condition as malignant disease than by waiting.

An illustrative case was that of a woman with outgrowths at various points of the larynx, from which pieces were taken on at least three occasions; each time the report was that no definite sign of malignant change was to be seen (fig. 9). Yet eventually malignant glands developed in the neck, with obvious carcinoma of the larynx.

Many other cases might be cited, among them the well known case of the Emperor Frederick of Germany. The difficulty has no doubt faced all laryngologists on many occasions.

Early involvement may be difficult to classify by biopsy. In a case which I observed after removal and section of the whole growth, obvious but localized malignant infiltration was seen (fig. 10). The area so affected was, however, small, and in the neighborhood no more than overgrowth of epithelium was seen, with but slight divergence in type from the parent prickle cells. Operation gave an excellent result.

At the other extreme, the growth may resemble sarcoma microscopically. Operation would be useless, as recurrence would be rapid; irradiation might, on the other hand, be expected to give improvement, at least for the time being.

The opposite mistake has occurred two or three times in my own experience; a report of carcinoma from microscopic examination has been made in cases of simple papilloma and of tuberculosis. The error lay, however, with the pathologist and not with the microscopic sections.

DIAGNOSIS OF THE DEGREE OF MALIGNANCY

Even if a diagnosis of carcinoma has been made, it may still be desirable and necessary to differentiate between the various degrees of malignancy, so that the most suitable method of treatment may be employed.

The age and general health of the patient, the rapidity of progress of symptoms, the extent and appearance of the growth and the possible invasion of the glands must be taken into consideration.

A young person—say below the age of 40—with a red, fleshy and rapidly growing neoplasm producing marked hoarseness may be found to have a growth placed in Broder's group 4. On the other hand, a man of 70 or 80 with a slowly progressing, whitish and nodular outgrowth causing no more than trifling hoarseness is likely to have carcinoma of group 1 or 2. Biopsy may decide the point and should afford a guide as to whether laryngofissure, total laryngectomy, interstitial irradiation or teleradiation is indicated.

I was associated with Sir St. Clair Thomson in the diagnosis and management of cases, some of which have been referred to in making this report. He also corrected this paper.

ACTINOMYCOSIS OF THE EAR

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HISTORY

Sixty years ago (in 1877), Bollinger and his botanist colleague Harz discovered and named the ray fungus, or Actinomyces bovis, the cause of a disease of cattle known as lumpy jaw, characterized by the formation of a hard, boardlike swelling of the tongue or a fusiform enlargement of the jaw. In the following year Israel described a similar mycotic disease in man, and in 1879 Ponfick suggested that the two diseases were identical. However, in 1891 Bostroem demonstrated the aerobic peculiarity of the organism found in 7 cases of actinomycosis in cattle, and coincidentally Israel and Wolff called attention to the anaerobic charcateristic of a similar branching organism isolated in 2 cases of the disease in man.

Organisms resembling Actinomyces have been isolated in several diseases. The fungus causing Madura foot, reported by Carter in 1874, was cultivated by Vincent in 1894 and shown to be an anaerobic branching, filamentous organism resembling A. bovis, which he called Streptothrix mandurae. Acid fastness in an anaerobic filamentous organism was first described by Nocard in 1888 (Actinomyces farcinicus). In 1890 Eppinger reported an acid-fast actinomyces in man.

There is evidence to show that one type of rat bite fever is due to a facultative aerobic member of the Actinomyces group, the Streptothrix muris ratti, isolated by Schottmuller (1914), Blake (1916), Tileston (1916) and others. In 1921 Henrici and Gardner isolated another acid-fast pathogenic species of Actinomyces, namely, Actinomyces gypsoides. Goldsworthy in 1937 reported a case of pulmonary actinomycosis caused by an acid-fast species of Actinomyces.

INCIDENCE

Actinomycosis involves the head and neck in nearly 60 per cent of the cases, according to Whalen, but its incidence in or about the ear is relatively slight. A total of 31 cases have been reported in the literature. Analysis of the reports shows that in 16 cases (51.6 per cent) the condition was confined to the external auditory canal and the pinna; in 15 cases (48.4 per cent) it involved the middle ear.

Presented as a candidate's thesis to the American Laryngological, Rhinological and Otological Society, Inc., April 27, 1938.

From the Oto-Laryngological Service, New York City Hospital, Welfare Island, Department of Hospitals, New York.

Actinomycosis in man is not a common disease. It is approximately twice as frequently found in men as in women, and the incidence is greatest in the third decade of life. The distribution of the primary lesion throughout the body, according to Leith's statistics, quoted by Pusey, is: head and neck, 52 per cent; abdomen, 21 per cent; lungs, 13 per cent; tongue, 4 per cent; skin, usually a secondary involvement, 2.5 per cent.

In spite of the rarity of actinomycotic infection in otologic practice several factors justify an awareness of its potentialities as a primary invader and as a secondary complication on the part of workers in this field. In the past far too many infections have been discovered at autopsy or too late for effective therapy.

The Wolff and Israel strain of Actinomyces appears to be a strict parasite; it has never been found outside the animal body, and its survival in artificial culture is brief. These facts suggest that the bovine type is transmitted by infected pus, saliva or nasal discharge (Topley and Wilson). The acid-fast species of Actinomyces, with other members of the genus, occurs as a saprophyte in soil or in vegetable matter and gains entrance to the body by being inhaled or through wounds (Henrici and Gardner).

BACTERIOLOGY

Topley and Wilson gave good reasons for including all the filamentous branching organisms in the Actinomyces group, although in some the proliferation of colonies takes on a definite ray structure, while in others the organisms form a felted mycelium without radial arrangement. These authors excluded from their classification of actinomycosis the granulomatous lesions of cattle and swine that are caused by organisms other than Actinomyces, distinguished between aerobic and anaerobic and introduced the important feature of acid fastness. The pertinent part of their classification follows:

CLASSIFICATION OF ACTINOMYCOSIS (Topley and Wilson)

A. Due to A. bovis of Wolff and Israel.
   Anaerobic. True ray fungus disease in man and cattle. Granules formed in tissues.

B. Due to aerobic types of Actinomyces.
   Aerobic.
   (1) Non-acid-fast group.
      (a) Granules formed in tissues, e. g., madura foot.
      (b) No granules formed in tissues, e. g., other lesions in man and animals.
   (2) Acid-fast group.
      (a) In man: chiefly pulmonary and abdominal infections. No granules formed in tissues.
      (b) In cattle: farcy. No granules formed in tissues.

C. Due to Actinomyces muris ratti.
   Rat bite fever (one type) in man and infective arthritis in mice. No granules formed in tissues.

In the department of pathology and bacteriology of the New York City Hospital four different aerobic non-acid-fast strains of Actinomyces which correspond to the organism of Scheele and Petruscky have been isolated from the blood stream. A review of the case follows:

CASE 1.—A white woman aged 30, with acute frontal sinusitis, septic fever (temperature of 104 F.) and acute arthritic manifestations, recovered.

CASE 2.—A white woman aged 54, with gallstones and a temperature of 102 F., was discharged improved without operation.

CASE 3.—A Negress aged 46, with hypertensive disease of the heart and a temperature of 102 F., was discharged improved.

CASE 4.—A white woman aged 34, with chronic active rheumatic disease of the heart, died. Autopsy confirmed the clinical diagnosis. No actinomycotic lesions identifiable as such were seen on histologic examination.

The acid-fast strains of Actinomyces are not common and therefore not as well known as other pathogenic varieties. Henrici and Gardner stated:

. . . they are, however, of great interest from the standpoint of bacteriology, since they furnish the closest contact between the true bacteria and higher fungi, being closely related to the tubercle bacillus in morphologic and cultural characters, pathogenicity and serum reactions; and, from the standpoint of clinical medicine, since they produce infections that bear a great resemblance to tuberculosis.

Of 670 cases reviewed by Sanford and Voelker, the condition was due to the acid-fast species in about 10. Clinically the disease is mainly a pulmonary infection. Metastases are common, and generalization progresses to some length before death. Such septicemic generalization was reported by Gammel in 1934 and by Fairley and Mackie in 1935, and Thjøtta and Gundersen reported the isolation of Actinomyces from the blood stream of a rheumatic patient.

The organism isolated in the case here reported had the characteristics of the aerobic acid-fast group (B,2,a); the case was the only one encountered in which an aerobic acid-fast organism has been isolated. The clinical report of the case with a description of the cultural characteristics of the organism follows:

REPORT OF A CASE

History.—J. F., an Italian man aged 42, a brick layer, was admitted to the New York City Hospital on March 3, 1933, and was discharged on June 30. He had had occasional colds, and mastoidectomy had been done at another clinic on Feb. 14, 1933; five days after operation frontal pain of a recurrent type developed, extending to the occipital region.

Examination.—A postauricular wound was seen on the left side; there was no discharge from either ear; the throat was injected and the chest and heart normal. The blood pressure was 120 systolic and 90 diastolic; there was no other

abnormality. The blood count on March 5 showed: leukocytes, 7,150; mature polymorphonuclears, 31 per cent; metamyelocytes I, 30 per cent; metamyelocytes II, 3 per cent; lymphocytes, 34 per cent; monocytes, 2 per cent, and no eosinophils or basophils. Otolaryngologic examination on March 7 revealed a slight serous discharge from the mastoid wound and tenderness on pressure over the posterior region behind the mastoid cavity. No sinal tenderness was observed; the patient complained of headache, accentuated at the time of elevated temperature and not localized except to the left side. The diagnosis was perisinal infection (abscess).

Operation.—In view of the septic fever temperature (99 to 104 F.) and the knowledge that the patient had had a mastoidectomy with probable exposure of the sinuses, operation was undertaken on March 8. The cavity of the previous mastoidectomy was exposed; numerous soft cells with granulations were found. The cells were removed and the sinus thoroughly exposed by the removal of the necrotic sinal plate. A specimen of pus from a localized area of periphlebitis ½ inch (1.3 cm.) in diameter was taken for culture. It was decided not to ligate or block off the sinus. The report on the culture showed nonhemolytic streptococci.

Second Operation.—On March 16 the sinus was again exposed; complete thrombosis of the sinus was found, extending from the bulb to within 2 inches (5 cm.) of the torcular Herophili. The clot was removed with suction, and the sinus was blocked; the internal jugular vein was ligated just above the facial vein. Material for culture was taken at operation, and the report, on March 21, showed hemolytic streptococci.

Postoperative Course.—After the operation a transfusion of 500 cc. of citrated blood was given. Altogether, four such transfusions were administered from March 16 to May 5, inclusive. There was leukocytosis, the white cell count ranging between 13,400 and 9,600 from March 8 to April 8. Healing of the wound was uneventful, but the patient had a low grade septic fever. On March 25 reports of blood cultures made on March 18 and 22 showed an acid-fast aerobic type of Actinomyces in the plate, in addition to hemolytic streptococci in the broth. Potassium iodide was immediately prescribed in ascending doses from 10 to 15 grains (0.65 to 0.97 Gm.) three times a day. No further colonies of Actinomyces were reported, and within two weeks the growth of streptococci first was retarded and finally ceased. On April 18 the patient complained of pain in the right sternoclavicular joint and the right shoulder and wrist. An increased daily peak temperature indicated resumption of sepsis. Administration of potassium iodide was stopped; dry heat was applied to the shoulder. A gonococcus fixation test on March 20 was reported negative. On March 22, 1 ounce (30 cc.) of thick yellowish pus was evacuated from the sternoclavicular joint. Culture showed hemolytic streptococci. Adequate drainage and a final transfusion on May 5 promoted recovery without further event. The patient was discharged on June 30 in good condition. Follow-up has shown no recurrence.

Bacteriology.—The acid-fast type of Actinomyces which was isolated from the blood stream in 1933 has been maintained as an acid-fast organism for four years at the time of this report on a modification of Sabouraud's medium described by Scudder, the formula of which is:

Beef heart infusion with sediment	1,000 cc.
Agar, flaked	20 Gm.
Maltose	40 Gm.
No adjustment for hydrogen ion concentration	
No peptone or salt	
Glycerin if preferred	

On this medium the acid-fast mycelium develops in three or four days and leaves as a residue in old cultures large oval sporelike acid-fast bacterial forms which are gram-positive and have the structure of coccoid bodies, although no true staphylococci have been isolated from the culture. The acid-fast characteristic has been inhibited on all other mediums, and no other strain of Actinomyces has exhibited the identical character of acid fastness. Best growth occurs at a temperature of 37 C. The organism conforms in biologic character to A. farcinicus, described by Nocard, although it liquefies gelatin when incubated from one to seven days at 37 C. Three distinct types of growth have been distinguished: (1) the

Fig. 1.—Four to seven day culture of the acid-fast type of Actinomyces on beef heart, 1.8 per cent agar and 4 per cent maltose, showing the crinkled grayish brown growth in which the acid-fast mycelium was first noted (1933).

creamy, translucent to yellow non-acid-fast type; (2) the creamy non-acid-fast type, becoming white and chalky with aerial hyphae; (3) the type that grows on the selective acid maltose medium, which proceeds from creamy to gray, to brown and to black and contains acid-fast portions. Pathogenicity has been established, although detailed work on the phases of growth and relative pathogenicity cannot be reported at this time. (Scudder, personal communication.)

The organism was grown on acid-fast medium no. 24861. Complete liquefaction of gelatin occurred in twenty-four hours at 37 C. No acidity was produced in

dextrose, lactose or saccharose. There was good cretaceous growth. The odor was fetid and unpleasant. Subculture on various mediums showed the following characteristics:

Medium	Characteristics
Potato	At first creamy to cretaceous; then changing to gray, to brown, to coal black.
Broth	Discrete fluffy colonies and a flaky pellicle if undisturbed.
Synthetic medium	Good growth, branching mycelium, creamy color.
Blood agar	Deep colony with a wide darkened area; no white powdery substance; surface colony dark, rough, translucent and nonhemolytic.
Veal agar	Colony at first round with smooth edge, then pitted and concentric; creamy to chalky.
Bordet-Gengou	Mustard yellow to very dark. Not acid fast; not cretaceous.
Favored medium (previously described)	Acid-fast mycelium in seventy-two to ninety-six hours.
Acid maltose	Acid-fast sporelike components in old culture; colonies at first creamy, leathery, round, translucent, becoming crinkled and pitted in the center, splitting and becoming chalky and then gray, brown and black.

The pathogenicity of the organism was not proved for the rabbit. In the guinea pig it produced abscesses of the chest and adhesions at the diaphragm. A gram-positive threadlike form containing gram-positive granules was demonstrated.

REVIEW OF CASES PREVIOUSLY REPORTED

Thirty-one cases of actinomycosis involving the ear are reviewed. The presence of ray fungi or the finding of Actinomyces determined the diagnosis in most of these cases, but in 3 cases no reports of such findings were specifically made. Of the 31 cases, the condition resulted in death in 16; in the other 15 complete or expected recovery was attributed to treatment by administration of iodine or iodides, surgical measures or roentgen irradiation, alone or in combination. Pertinent features of all the cases follow:

1890: Ginsberg (cited by Drury, by Jacoby and by Vielle) reported Actinomyces in a parotid fistula, which improved under treatment but was complicated by cervical and facial swelling, with the development of persistent paralysis of the facial nerve. Later there were severe pain in the left side of the head, dilated pupils and papillary edema. The patient failed rapidly and died. At autopsy actinomycotic granules were found in the left ear and mastoid and in the left temporal bone.

1892: Majocchi (cited by Beysiegel, by Drury, by Vielle and by Hagemann) reported a case of chronic otitis media with terminal symptoms of cerebral involvement. Autopsy revealed partial destruction of the wall of the labyrinth, purulent meningitis and sinus thrombosis. Pus in the middle ear and in the bone contained actinomycotic granules. There was also an actinomycotic infection of the lungs and pleura, which Beysiegel suggested was secondary to that in the ear.

1893: Dor (cited by Vielle) reported the case of a woman who had been kicked in the face by a cow, which caused a submaxillary swelling that extended

upward. Fistulas developed, one of which opened into the external auditory canal; the condition was diagnosed as actinomycosis. The patient died of pulmonary generalization.

1894: Zaufal (cited by Beysiegel and by Beck in the American literature) reported a case of actinomycosis of the middle ear and the mastoid, with subsequent involvement of the parotid region. Meningitis developed, and autopsy showed extension of actinomycotic infection from the petrous to the occipital bone, which undermined the dura and eroded the left vertebral artery. The ray fungus was demonstrated.

Fig. 2.—Culture of the same organism in the fall of 1937, on the same kind of medium, showing definitely at least two phases of growth: *A*, the crinkled yellow opalescent non-acid-fast colonies and, *B*, the crinkled chalky darkening type of growth in which the acid-fast mycelium develops.

1895: Poncet (cited by Vielle and by Drury) reported the case of a man aged 54 who had an actinomycotic tumor in the parotid region, alveolar periostitis and gingival abscesses. All affected areas discharged material containing fungi, and later there was a discharge from the ear containing Actinomyces. This man stated that he had habitually chewed bits of straw. Treatment with iodide resulted in cure.

1896: Poncet's second case (cited by Vielle) was that of a man aged 64 who had a swelling in the left parotid region extending below the orbit, with several

fistulas. The left ear discharged intermittently, and the external canal was filled by a swelling. There was paralysis of the superior branch of the left facial nerve. Incision below the orbit revealed small cavities containing actinomycotic granules. A second incision in front of the ear yielded pus and granulations.

1896: Von Bonsdorff (cited by Beysiegel) attributed the actinomycotic infection in his case to a grain of corn which the patient, a farmer, had thrust into the meatus. A few months later, at operation, pus containing a remnant of grain and typical granules was found in the external auditory canal. The condition responded to surgical treatment.

1896: Ten Siethoff (cited by Beysiegel and by Hagemann) gave credit to potassium iodide for the recovery within four weeks of a patient with actinomycosis of the external auditory canal, with superficial mastoid involvement and

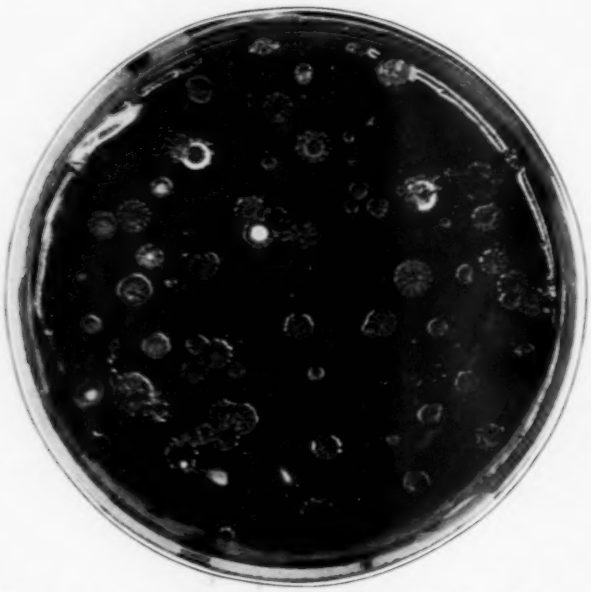

Fig. 3.—Pour plate on beef heart agar without blood and of a slightly acid reaction, made from an old (October 1937) culture, from which the two types of colonies in figure 2 were fished. The colonies are concentrically arranged, with chalky white aerial hyphae developing at their centers.

extension along the sternocleidomastoid muscle. In the pus actinomycetes with granules were found.

1896: Reinhard (cited by Beysiegel and by Hagemann) demonstrated Actinomyces in the pus of a burrowing cervical abscess following mastoidectomy, characterized by hard infiltration without fluctuation. Surgical measures were undertaken.

1901: Littledale reported actinomycosis of the external ear in a man aged 23. Swelling began at the lobule of the left ear, and extended forward and downward. Discharging pus containing actinomycotic granules developed in several sinuses. The lungs were later involved, but no involvement of the middle ear was noted either clinically or pathologically. The patient died.

1901: Poncet's third report (also cited by Vielle) described actinomycosis of the lobule of the ear of a woman aged 53. Early arrest was secured without involvement of bone, and the patient's general health was good. The condition was treated with iodine, with recovery.

1903: Vielle traced the condition in his case to the extraction of a wisdom tooth, with infection in the mouth and formation of an abscess, which opened spontaneously. Later a discharge from the left ear and swelling of the left side of the jaw occurred. Incision of the swelling revealed a cavity filled with granulations, which proved to be actinomycotic, as did the pus discharged from the

Fig. 4.—High power magnification of four day culture grown on acid maltose, stained with carbolfuchsin. The colony is grayish brown. Acid-fast portions of mycelium have developed.

ear. Vielle regarded this case as one of actinomycosis of the external ear, as there was no diminution of hearing and no tenderness over the mastoid. Iodine dressing was used.

1904: Rivière and Thévenot's case was one of primary actinomycosis confined to the external ear in a man aged 36. Pain in the left ear, discharge of pus and diminution of hearing directed attention to an external canal filled with granulations and a thickened but imperforate tympanum. Pain and swelling developed over the left mastoid and sternocleidomastoid regions. Incision revealed small

abscesses, which were curetted and treated with iodine. The bone was not involved. Actinomyces were found only in the discharge from the ear.

1906: Pochon reported a case of lobular actinomycosis in a girl aged 14 whose ears had been pierced for earrings. Hard swelling developed, with several small fistulas, in the discharge from which actinomycotic granules were found. The condition was treated with local applications of radium and with potassium iodide by mouth.

Fig. 5.—High power magnification of one week culture grown on an acid medium, stained with carbolfuchsin. Acid-fast beaded filaments and acid-fast spores have appeared.

1910: Pinaroli demonstrated actinomycetes microscopically in the pus from a patient with "acute otitis" who recovered in five weeks under iodine treatment. A peculiar feature of the case was the acute course, unusual for actinomycosis.

1910: Urbantschitsch described a case in which actinomycetes appeared in the discharge from a fistula extending into the mastoid process from a purulent external auditory canal. The tympanic membrane was not perforated. In this case the trouble started with an edematous swelling of the entire left cheek, eyelid and retromandibular region. The skin was reddened, covered with crusts and penetrated by numerous small fistulas. There was hard infiltration in the parotid-

masseteric region, with fistula formation in the lower jaw. Surgical intervention was followed by recovery.

1915: Wegelin reported a case of actinomycotic meningitis in which autopsy revealed pus containing specific granules in the right eustachian tube and middle ear resulting from a primary focus in the jaw.

1920: Corinth likewise reported a case of fatal suppurative meningitis in which actinomycotic granules were seen at autopsy in a "granulation tumor" of the right gasserian ganglion. Purulent otitis media suggested the portal of entry, but the report did not mention the finding of granules in that region. The patient was 28.

1922. Bruzzone reported temporomastoid actinomycosis in a man aged 48. "Septo-pyemia" resulted in death. No pathologic or bacteriologic details were given.

1925: Döderlein reported an interesting case of actinomycosis of the middle and the internal ear in a boy 4¾ years of age in which autopsy revealed that the infection had apparently reached the meninges by traveling along the course of the acoustic nerve, since there was no destruction of the inner portion of the temporal bone. During the previous year there had been an occasional discharge from the right ear, without other symptoms. Convulsions suddenly developed, and the child became unconscious. There were definite signs of meningitis on admission to the hospital. The right tympanic membrane was reddened and bulging in the posterior portion. The antrum was opened. All the exposed mastoid cells and the antrum were filled with granulations, which differed in appearance from those usually seen in cases of chronic otitis media but contained no actinomycotic granules such as were found in the fluid pus from the labyrinth.

1925: Voss reported 3 cases, of a boy, a man and a woman, in all of which actinomycosis of the external auditory canal developed from an initial lesion of the cheek. In 2 of these the condition responded to roentgen therapy; in the third roentgen irradiation and administration of potassium iodide did not produce recovery.

1928: Rockemer and Wirth reported a case of infection of the middle ear, probably actinomycotic although not definitely proved so, in a woman aged 56. She had had recurrent discharge from the right ear for several years, which had recently increased, accompanied with pain and the development of an abscess in the right supraclavicular fossa [sic]. She had had fever on admission. Although there was no tenderness over the mastoid, a radical mastoidectomy was done. A large cavity filled with pus was found, with destruction of the posterior wall exposing the dura and the wall of the sinus, which showed a yellowish color. The sinus pulsated only on pressure. Repeated blood cultures were made before the patient died twenty days later. Both aerobic and anaerobic cultures were sterile. The pus from the abscess opened at operation showed no granules, but did reveal gram-positive filaments with clubbed ends, not acid fast, which in their arrangement and appearance resembled Actinomyces more closely than any other form of Streptothrix. The patient died.

1929: In Drury's case the condition followed the removal of teeth. Superficial abscesses developed around the ear, and a partial mastoidectomy was performed when signs pointed to obstruction of the middle ear. Pus and granulations were found. At a third operation most of the remaining mastoid bone was removed. The patient died of meningeal involvement. Typical actinomycotic granules were demonstrable on only one occasion noted in the report.

1929: Zanni described a case in which actinomycosis of the external auditory canal responded promptly to treatment with iodine and potassium iodide. A man aged 40 had pain and a discharge from the ear; the pain subsided but the discharge

persisted; no relief resulted from paracentesis. A retroauricular swelling developed, which finally formed a fistula. This lesion disappeared under local applications of iodine. A small granulation was found in front of the tympanic membrane and removed. Granules, shown by microscopic examination to contain actinomycetes, were repeatedly found in pus from the ear and in the discharge from the fistula. Ten days' treatment with potassium iodide resulted in recovery.

1931: Cann and Hollis reported cerebral actinomycosis in a 9 year old girl, which was revealed at autopsy to have originated in the ear, since "Careful search failed to disclose any other possible primary lesion beside the middle ear." Thick yellow pus "filled the middle ear"; the drum was intact, and "there was no evidence of involvement of mastoid cells." No symptoms were present in the ear during life, but granules containing masses of mycelium were demonstrated in the cerebrospinal fluid in two specimens. Postmortem specimens of pus from the middle ear and from the meninges also revealed mycelium when cultured anaerobically in dextrose broth.

1933: Beysiegel reported the case of a woman aged 18, in whom painful swelling developed in the external auditory canal and behind the right ear, with a history of swelling of the lower jaw which was unrelieved by the removal of a wisdom tooth suspected of being a focus of infection. Roengten examination revealed no changes in the mastoid, but the swelling behind the ear was widely opened, and a narrow cavity filled with pus and lined with granulation tissue was found. Actinomycetes were demonstrated in the granulation tissue but not in the pus. The condition ultimately cleared under local roentgen irradiation and administration of potassium iodide by mouth.

1933: Hagemann reported a spontaneous rupture of a postauricular abscess in a man aged 36. Throbbing pain developed in the left ear, with tenderness over the mastoid. Roentgen examination showed transparencies in the mastoid bone, and a mastoidectomy was performed, revealing a thickened and somewhat reddened sinal wall. As the wound healed, swellings developed above the ear and in the neck. These were incised and pus secured, which contained numerous actinomycotic granules. The patient was discharged much improved after roentgen irradiation and did not report again.

1937: Barth described recurrent attacks of otitis media in a woman aged 29, on whom a mastoidectomy had been done when an acute attack was accompanied with paralysis of the abducens nerve and trigeminal neuralgia. No abscess was found. A second operation revealed nothing of significance. Death occurred ten days later, and autopsy revealed basal suppurative meningitis. A subcutaneous cervical abscess had developed just before death; the pus from the abscess and from the ear showed actinomycosis.

1937: Nehmer reported a case of paralysis of the left side, with a fluctuating swelling in the right parietal region, from which sterile pus was secured before the patient died. At autopsy an abscess of the right temporal lobe, granulations and pus in the mastoid cells and tympanic cavity and intact bony walls of the labyrinth were revealed. Typical actinomycotic granules were found in the granulations in the mastoid and middle ear. Areas of inflammation were noted at the tympanic orifice of the eustachian tube, but no actinomycetes were demonstrated in these lesions. Nevertheless, Nehmer's conclusion that the infection reached the middle ear and mastoid via the eustachian tube seems justified, there being no record of infection of the temporal bone due to generalized actinomycosis with dissemination through the blood stream.

COMMENT

Wilkinson reported granules resembling those of actinomycosis in 1.17 per cent of 10,000 pairs of tonsils systematically examined at the Mayo Clinic between 1923 and 1927. Drury traced the origin of the condition in his case to the removal of infected teeth. The ray fungus has a predilection for connective tissue and extends principally by continuity, but other tissues and contiguous structures are by no means immune to invasion.

Vielle expressed the opinion that the infection usually spreads through the eustachian tube; the organism may remain in the nasopharynx for some time, especially in the region of the tonsils, without producing any lesion; coughing may force the organism through the tube into the middle ear, which explains the cases of primary actinomycosis of the middle ear. As in Majocchi's case, secondary infection of the ear may be caused when bronchial secretions containing actinomycetes are coughed up into the nasopharynx.

Infection of the middle ear may result from the involvement of the external ear in cases in which a previous perforation of the drum is present, or the drum may be injured by some foreign body and the fungus introduced at the point of injury.

The possibility of infection of the ear from a distant focus by means of "actinomycotic embolism" is noted. Vielle, however, stated the belief that there is little probability of such an occurrence. While occasionally the spread of actinomycotic infection by the blood stream has been observed, the parasite rarely invades the arteries. Even if present in the blood stream, it would have difficulty in entering the tympanic cavity, owing to the small caliber of the blood vessels there. Furthermore, it would be necessary to attribute a power of selection to the embolus to suppose that it would leave the carotid to pass into the internal maxillary artery and select among the branches of this artery the tympanic branch or the auricular branches of the meningeal artery to reach the cavity.

Rivière and Thévenot noted that actinomycosis of the external ear is a form of cutaneous actinomycosis and rare. They added that infection may be carried to the ear by the blood stream, but this would hardly occur except with a generalized infection by actinomycetes with multiple lesions (pyemia).

Beysiegel observed that the portal of entry in cases of actinomycosis of the ear is uncertain; in some cases the infection may extend from the mouth through the parotid; definite proof of infection by way of the eustachian tube is difficult to obtain, yet this is usually supposed to be the route when no other method of infection can be demonstrated. Occasionally infection may occur from the external canal. Beysiegel

remarked that symptoms of actinomycosis of the middle ear are slight and usually develop late and only when the disease has extended so far that treatment is of little avail. Resistance to treatment may continue until intracranial complications develop without actinomycetes being found in the primary focus.

Döderlein remarked on the few symptoms attending extensive involvement of the middle ear and labyrinth, the symptoms becoming acute only when the infection reaches the meninges. He expressed the opinion that infection in his case reached the middle ear by way of the eustachian tube. Since there were no lesions in the nasopharynx, the case may be considered one of primary actinomycosis of the middle ear and labyrinth.

Nehmer's case illustrated the eustachian portal of entry in cases of infection of the middle ear and served to emphasize the importance of carefully examining the granulations in order to demonstrate the presence of Actinomyces.

Takahara reported experiments on rabbits in which actinomycetes from chronically diseased tonsils were introduced into the tympanic cavity, the common carotid and the vertebral artery. In the tympanic cavity the fungi increased in the first month; in the second month typical clubs were formed; in the third month typical granules appeared. Labyrinthine or intracranial complications developed in some instances three months to a year after the infection of the tympanic cavity. When the actinomycetes were introduced into the arteries, pathologic changes characteristic of actinomycosis were found chiefly in the lungs. The normal ear was not infected by the hematogenous route in these experiments.

Friedman, Plaut and Levy reported a case of actinomycosis of the central nervous system in which lesions were found in both the spinal cord and the brain. The left middle ear in this case contained "thin, bloody fluid"; greenish yellow or yellowish pus was present in the base of the brain and in the hypophysis. No mention was made of any definite involvement of the ear in this case, but the authors stated that in a review of the literature they found 6 cases of cerebral actinomycosis due to extension from the middle ear.

The organism of Wolff and Israel was probably the offending organism in most of the cases reviewed, but the cultural characteristics of the actinomycetes isolated were not described in all cases. The question always arises whether the actinomycetes isolated in the various cases are merely accidental contaminants of no significance or definitely pathogenic.

Waksman, in his study of the cultural characteristics and metabolism, found that the species of Actinomyces are not fixed as to physiologic characteristics or structure, are not differentiated by liquefaction, fer-

mentation of carbohydrates and other usual cultural characters and are only superficially different as regards parasitism and saprophytism.

Gordon and Hagan reached the conclusion from their investigations of acid-fast actinomycetes that they

> . . . have not found any features that will serve to distinguish the "pathogenic" types from the "soil" types. The character of the pigment formed will distinguish some strains from others; however, both "pathogenic" and "soil" types are usually pigmented, the colors ranging from yellow through orange to coral.

TREATMENT

Iodides have been used with some success in cases of infection with the non-acid-fast variety of Actinomyces. Their usefulness against the acid-fast variety is more doubtful. Henrici and Gardner stated the belief that their administration is of doubtful value, since in cases of pulmonary tuberculosis, an infection with an acid-fast organism, disastrous results have been reported. The application of iodine locally whenever possible is advised, as is the use of potassium iodide in daily ascending doses. Roentgen irradiation and autogenous vaccines have been successfully employed in some cases.

SUMMARY

The literature of actinomycosis of the ear is reviewed.

A case of acute mastoiditis complicated by sinus thrombosis, septicemia and arthritis in which an aerobic acid-fast type of Actinomyces was isolated from the blood stream is presented.

It is suggested that, in spite of the rarity of actinomycotic infection in otologic practice, several factors justify an awareness of its potentialities as a primary invader and as a secondary complication on the part of workers in this field.

The method of treatment is still questionable in cases of infection due to the acid-fast types.

Both aerobic and anaerobic types of Actinomyces are capable of producing lesions in man, but it is impossible to distinguish the pathogenicity of the types bacteriologically.

It is suggested that the organisms gain entrance to the middle ear (1) through the eustachian tube or (2) by continuity.

Dr. James Lisa and Miss Sara A. Scudder, of the Department of Pathology and Bacteriology of New York City Hospital, assisted in the preparation of the bacteriologic material in the case reported.

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TISSUE CULTURE OF NASAL CILIATED EPITHELIUM

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Not much is known of the factors which determine the growth, regeneration and health of the nasal epithelium. Such knowledge, when once obtained, will axiomatically be of first importance, not alone in the treatment of nasal infections but in the prevention and the early abortion of many air-borne diseases. If means were at hand to hasten the regeneration of epithelium after some organism has succeeded in breaking through it, secondary invasion might be effectively restricted.

Three facts, only relatively recently established, have stimulated us in an attempt to learn more about the characteristics of growth of the nasal and the sinal mucosa: (1) that after complete removal the mucosa of a sinus can be regenerated with normally functioning ciliated columnar epithelium;[1] (2) that in clinical practice this regeneration is not invariable, and (3) that normal vigorous ciliary activity usually—in fact, almost invariably—exists within a sinus even in the presence of overwhelming infection of long standing.[2]

To account for the last, two possible explanations occur to one: Either the infection in its acute stage destroys the epithelium, which is later regenerated in spite of the persistence of the infection in the deeper layers of the mucosa, or the organisms penetrate to the deeper layers only at scattered points, invading the tunica propria and leaving the greater part of the epithelium intact. There is evidence to be had from fixed and stained sections of tissue in support of either view.

The experiments in tissue culture which are the subject of this communication have been undertaken in the hope of discovering in the behavior of the living tissue something which may be clinically useful in preserving intact epithelium in the nose and in expediting its repair when once it has been injured.

The literature on the subject is almost nonexistent; although experiments with other epithelium abound, they are not sufficiently closely related to be of much help. The epidermis of the frog has been grown.[3]

From the Oscar Johnson Institute, Washington University School of Medicine.

1. Knowlton, C. D., and McGregor, G. W.: How and When the Mucous Membrane of the Maxillary Sinus Regenerates, Arch. Otolaryng. **8**:647 (Dec.) 1928.

2. Proetz, A. W.: Studies of Nasal Cilia in the Living Mammal, Ann. Otol., Rhin. & Laryng. **42**:778 (Sept.) 1933.

(Footnotes continued on next page)

Strelin [4] reported a culture of bronchial epithelium from a rabbit, but the period of growth was short (nine days), and the author's conclusions therefore seem to us somewhat incomplete. Carleton,[5] working with late fetal cat and rabbit bronchi, was unable to maintain ciliary growth in vitro. Vogelaar [6] noted growth of epithelium in cultures of material from the human thyroid gland. We failed, however, to uncover any mention of an attempt to grow nasal cilia; hence there was nothing to suggest to us the proper medium for their proliferation.

Since the main purpose of our study was to obtain knowledge of growth-controlling factors which might subsequently be applied clinically, it seemed important to resort, for both mediums and feeding solutions, to substances of known composition.

In this respect, the medium devised by Vogelaar and Erlichman,[6] seemed especially suitable; moreover, one type of mammalian epithelial tissue had already been made to grow on it.

Practically from the beginning some growth was obtained in this medium. We published a preliminary report of the early experiments in 1936.[7]

However, certain minor modifications in the medium were required before it was adequate for the purposes of the experiment. At first only thin strands of epithelial cells could be grown, which, while covered with active cilia, were extremely fragile and did not sufficiently simulate the nasal epithelium in the arrangement of cells to be of much value. Later it became possible to grow epithelial cells in sheets and to observe something of the character of their growth and proliferation.

CULTURE TECHNIC

PREPARATION OF MATERIAL

The tissue used in these experiments was the mucosa of the turbinates and septum of guinea pig fetuses at term, chosen in order to avoid the bacterial contamination which occurs as soon as the animal has

3. Uhlenhuth, E.: The Form of the Epithelial Cells in Cultures of Frog Skin and Its Relation to the Consistency of the Medium, J. Exper. Med. **22**:76, 1915.

4. Strelin, G. S.: Ueber in-vitro-Kulturen der Bronchen des Kaninchens mit besonderer Berücksichtigung des Epithels, Arch. f. exper. Zellforsch. **9**:297 (April 8) 1930.

5. Carleton, H. M.: Growth, Phagocytosis and Other Phenomena in Tissue Cultures of the Foetal and Adult Lung, Phil. Tr. Roy. Soc., London, s.B **213**:365, 1925. Chlopkow, A. M.: Intestinal Epithelium of Adult Rabbit Cultures in Vitro, Arch. f. exper. Zellforsch. **10**:299 (Feb. 16) 1931.

6. Vogelaar, J. P. M., and Erlichman, E.: A Feeding Solution for Cultures of Human Fibroblasts, Am. J. Cancer **18**:28 (May) 1933; The Growth of Human Fibroblasts in Media Containing Silver, ibid. **22**:555 (Nov.) 1934; Some Remarks on the Growth of Human Fibroblasts in Media Containing Copper, ibid. **22**:66 (Sept.) 1934.

7. Proetz, A. W., and Pfingsten, M.: Ciliated Nasal Epithelium: Its Culture in Vitro; Preliminary Report, Ann. Otol., Rhin. & Laryng. **45**:400 (June) 1936.

breathed. This is no longer strictly embryonic tissue, as the period of gestation has been completed.

Removal of Embryos.—The skin of the abdomen is raised with dissecting forceps, cut through along the midline from the sternum to the pelvis, reflected on both sides and clamped. With fresh instruments the abdominal muscles are raised and cut along the midline through the abdominal wall so as not to injure the intestines or the uterus. Through a small incision in the uterine wall the embryos are removed one by one with a hemostat. The umbilical cord is cut, and each animal is placed in a sterile container with a small amount of Locke or magnesium-Ringer solution to prevent drying.

The jars containing the embryos are placed in a glass cage, which is used both for dissecting the embryos and for preparing the cultures. The cage, constructed of wood and plate glass, has along the front an opening covered with overlapping sheets of rubber. A small wooden door closes the remainder of the front opening, which facilitates the introduction and removal of instruments and dishes. The operator works with sterile hands through the rubber front, which permits remarkable flexibility of movement. The cage greatly lessens the likelihood of bacterial contamination from air currents and prevents breathing on the tissue during the manipulations. With this cage and a careful technic, our cultures are seldom contaminated.

Obtaining of Blood.—In these experiments plasma from the animal from which the embryos were taken has been consistently used. It is essential that the plasma be obtained under strictly aseptic conditions. The pregnant guinea pig is prepared surgically and bled to death directly from the heart. A triangular flap of skin is made from the base of the sternum—the skin being reflected upward on both sides to the forearms—and is clamped with a hemostat. With scissors and forceps the base of the thorax is cut at the junction of the diaphragm with the sternum. The ribs are then cut through on each side of the sternum. The sternum can then be reflected upward toward the neck and the heart exposed. It is necessary to work rapidly and carefully in order not to injure the lungs or large vessels. The needle (20 gage), attached to a 15 cc. syringe and previously rinsed with solution of sodium citrate, is introduced into the left ventricle of the heart. According to the size of the guinea pig, it is possible to obtain from 8 to 15 cc. of blood.

Preparation of Plasma.—The blood is placed in sterile centrifuge tubes containing solution of sodium citrate. One-half cubic centimeter of an 8.3 per cent solution of sodium citrate in distilled water per 10 cc. of blood prevents clotting. The blood is thoroughly mixed with the solution and is then centrifuged at high speed for ten minutes. With sterile pipets the plasma is removed and stored in tubes in the refrigerator until ready for use. This step in the preparation of the plasma may be carried out before or after the removal of the embryos but preferably afterward.

Dissection of Embryo.—The instruments and towels are arranged within the cage. Several small covered dishes containing Locke or magnesium-Ringer solution at 37.5 C. are required to receive the freshly dissected tissues. One by one the embryos are lifted on a Petri dish for support. A median incision is made from the tip of the nose to the back of the neck, after which the skin is reflected and clamped on either side with two small hemostats. After the periosteum is elevated, another median incision is made through the soft nasal bone down to the septum, and the right and left nasal bones are lifted off with forceps. After the removal of both turbinates and the stripping of the epithelium from the septum, these tissues are transferred immediately to the Locke solution.

With fine dissecting forceps the posterior end of the turbinate is grasped, and with sharp manicure scissors minute pieces of epithelium are clipped from the turbinate. The epithelium from the septum also is cut into small pieces (from 0.5 to 2 mm.; not more). The fragments are kept in Locke solution, ready for implantation.

CULTURE

Preparation.—In preparing the cultures the hanging drop technic is used, with large Maximow slides and glass or mica cover slips. The Carrel flask technic also has often been used, but for photographic purposes the slide technic has been more satisfactory. The cultures are made within the cage by using, according to the exact specifications of Vogelaar, equal proportions of plasma, calcium-Ringer solution and feeding solution. This produces a firm clot in five to ten minutes.

The solutions are mixed together in a test tube. The culture medium is then transferred to the cover slips with a capillary pipet. The minute fragments of tissue are handled with cataract knives and placed in the medium just before clotting or on the surface while the clot is forming. Two to four fragments are placed in a single culture. The large Maximow slides, previously rimmed with petrolatum, are placed over the slips, and when the clots are firm the slides are inverted, sealed with paraffin, and incubated at 37.5 C. When liquefaction occurs, the cultures must be refed or transplanted, according to the amount of growth.

Medium.—The feeding solution devised by Vogelaar contains magnesium-Ringer solution, peptone, thyroxin, hemin, cysteine hydrochloride, dextrose, insulin, and the acid phosphates of sodium and potassium. For details of preparation, the reader is referred to the articles of Vogelaar. The magnesium-Ringer solution contains sodium, potassium and calcium chloride plus sodium bicarbonate and magnesium sulfate. The calcium Ringer solution contains sodium and potassium chloride plus an increased amount of calcium chloride.

From time to time we have modified the medium by replacing the feeding solution with extract of guinea pig embryo or by using the extract in conjunction with the feeding solution and reducing the amount of the feeding solution one half. The objection to the use of embryo extract is that its exact chemical formula is unknown. It produces a firmer clot, which has proved to facilitate the production of epithelial sheets. Furthermore, in a firm clot liquefaction progresses less rapidly.

Uhlenhuth [3] has shown that in cultures of frog skin the consistency of the medium was a factor in determining the character of epithelial growth. In a firm medium the cells were permanently polyhedral and maintained a compact membrane, while in a soft medium the cells were fusiform or filiform, and migration of isolated cells occurred. External factors may cause changes of form as well as functional changes in the cells themselves. In our experiments only guinea pig plasma has been used.

Embryo Extract.—Embryo extract is prepared by mincing young guinea pig embryos and diluting the pulp with one-half portion of Locke or magnesium-Ringer solution. It is then centrifuged several times, and the clear supernatant fluid is transferred to sterile storage tubes until ready for use. The extract can usually be kept from eight to ten days in the refrigerator.

STAINING

It is often desirable, in order to keep a permanent record of the characteristics of growth, to interrupt some of the cultures at various stages and stain the

tissues. We have found the simple methylthionine chloride technic of Fischer to give good results. The Giemsa stain is also satisfactory, as it can be readily washed from the clot.

In our experiments to date we have used 44 pregnant guinea pigs. The average number of cultures prepared at each time was 25. Sometimes a larger number of cultures was prepared, when the quantity of the material and conditions were favorable. These observations, therefore, are based on over 1,100 normal cultures.

PHOTOGRAPHY

The photographing of the cultures has a purpose beyond the mere record. In its nature the experiment is progressive, and it is necessary to preserve the details of each stage of the progression in order to form some conception of it as a whole.

Two types of photographs are now being employed: series of stills and motion pictures. Beside furnishing a vivid record of the action, which may be repeated and studied at leisure, motion pictures have the advantage that, through proper manipulation, growth of a culture requiring several days may be represented as occurring in only a few minutes.

STILLS

The still photomicrographs were made in the usual manner and require no comment. The motion pictures, however, owing to the liquid nature of the culture and the close proximity of the laboratory to street traffic and a railroad, required special apparatus.

APPARATUS FOR CINEMICROGRAPHY

The microscope, in an incubator, stands on a vibration-proof table. This table consists of an exceptionally heavy wooden top clamped on pillars composed of dissimilar layers of concrete, rubber and cork in such a manner that any slight remaining tendency to periodic vibration in one pillar will be neutralized by the others. The whole apparatus stands in a pit dug in a subbasement, where it has no contact with the floors and walls of the building.

An improvised switching device, consisting of two cams driven by a synchronous electric clock motor, turns up the light, trips the camera and shuts off the light. This cycle is repeated at desired intervals, resulting in an apparent speeding up of the action from 320 to 960 times.

The camera is suspended from the ceiling and is not in contact with the microscope; thus is avoided the transmission of any vibration to it. The entire apparatus has been described in detail.[8]

OBSERVATIONS

CHARACTERISTICS OF GROWTH OF TISSUE

A few observations have been made at this writing of the cultural characteristics of the tissues studied.

8. Proetz, A. W.: Motion Pictures of Tissue Cultures (Ciliated Epithelium), J. Biol. Photographic A. **6**:84 (Dec.) 1937.

In each case the implant was a fragment of epithelium removed from the nose, usually a turbinated body, with a small mass of fibroblasts adhering to its under side.

There is a tendency for the edges of the epithelium to curl under, and sometimes around the fibroblasts. When this occurs and there is no free edge, the epithelium does not grow.

Growth may be apparent as early as the second day but usually begins on the third or fourth day. After an incubation period of a few hours, migrating cells often emerge from the fragment and may surround it in a rather dense zone.

Regardless of whether growth is apparent, liquefaction of the medium where it is in contact with the epithelium begins practically at once. The fibroblasts grow out from the implant in radiating strands and penetrate the medium for some distance and for some time (two to three days) before liquefaction takes place.

The amount of liquefaction appears to be increased when the growth is rapid. The new cells may live for some time in the liquefied medium but do not multiply and eventually die unless the medium is changed.

When the epithelium grows in thin strands and to a lesser degree when it grows in sheets, the distal cells cling to the receding wall of the medium (receding because of liquefaction) or to any débris which may be there. The epithelium spreads also along the surface of this wall in a sheet. When the wall recedes faster than the tissue grows, the strand of cells is broken. With the firmer, more slowly liquefying medium this does not occur.

In our epithelial cultures, many of which were cultivated from three to four weeks, there was never any difficulty in distinguishing the epithelial cells from the fibroblasts. We can thoroughly agree with Ebeling and Fischer[9] that when epithelial cells and fibroblasts are growing together in the same medium they both maintain their individual characteristics. The epithelium, whether growing in tubular formation or as a sheetlike membrane, always tends to grow more compactly, with the individual cells closely adherent to one another. The typical network of the fibroblasts is always evident. Membrane-like or sheetlike growth of the epithelium is rapid, more so than tubular growth. We have not seen the dedifferentiation described as occurring in related tissues. The growth and migration of epithelial cells seem to be more

9. Ebeling, A., and Fischer, A.: Mixed Cultures of Pure Strains of Fibroblasts and Epithelial Cells, J. Exper. Med. **36**:285 (Sept.) 1922. Fischer, A.: Tissue Culture: Studies in Experimental Morphology and General Physiology of Tissue Cells in Vitro, in Contributions from the University Institute for General Pathology, Copenhagen, Levin & Munksgaard, 1926, vol. 4, p. 99. Erlichman, E.: Human Fibroblasts Grown for a Year in a Medium of Sheep Plasma and Two Solutions of Known Composition, Am. J. Cancer **24**:393 (June) 1935.

dependent on the mechanical conditions of the clot than are those of the fibroblasts.

Local changes in surface tension of the medium may account for many of the varying patterns of growths.

Small bits of cartilage often adhere to the epithelial fragments. One culture showed an extensive bridge of ciliated epithelium connecting two fragments of cartilage, one of which had an adherent piece of membrane anchored to the clot of plasma. On the opposite side fibro-

Fig. 1.—Photomicrograph of culture of tissue from the nasal mucosa of the guinea pig. At the upper right is the implant, with fibroblasts growing away from the center and ciliated epithelium growing toward it. The extent of liquefaction is outlined by the circle. A thin strand of epithelial tissue reaches down from the implant and is attached by a fan-shaped mass to the margin of the liquefied medium.

blasts and large flat epithelial cells were growing. This was in a seven day culture.

Ciliary motility on individual epithelial cells, which have wandered or possibly have regenerated from a small clump of cells far removed from the original fragment, can frequently be seen. The vitality of these isolated cells is great. Often they assume a spherical form and

are covered on all sides by cilia. Sometimes they are caught in the meshwork of fibroblasts.

The epithelial cells usually develop a yellow cast. Mitochondria in individual cells are often visible in the cytoplasm in the form of fine rodlike structures. The epithelial cells usually contain a large number of minute refractile granules.

The promptness with which ciliary activity appears on the surfaces of new cells is amazing. Approximately four fifths of the sheet of

Fig. 2.—Implant lying at the border of liquefaction. The strand of new epithelial tissue running off the field to the left is covered with active cilia.

new cells is in active motion in all the specimens. The actual time of the appearance of activity varies with the rapidity of growth of tissue.

It has been observed also that ciliary activity comparable to that in the adult is found in the guinea pig as early as at one-third term, or after about three and one-half to four weeks of a sixty-three day gestation.

Carleton [5] has stated that in cultures which he made of the larger bronchi in later periods of fetal life (cat or rabbit) when cilia were

present they disappeared in vitro. He reported that the farther the cells grew from the parent epithelium the less they resembled it. This is not in accord with our observations. As previously stated by us, the new epithelial cells are covered with active cilia, whose motion and speed of vibration cannot be distinguished from those of the parent cells.

With time lapse photography, at an apparent acceleration of 960 times, definite characteristics of growth may be observed. The epithe-

Fig. 3.—In this culture the new growth extending down and to the left forms a sheet, and there is less liquefaction. Fibroblasts are seen growing upward at the upper right.

lial cells appear to stretch in the direction of growth of the general mass and then to contract again to their previous shape and position. They do this a number of times before the cells divide. Growth proceeds along what appear to be extremely slender protoplasmic threads, first sent out by the cell in the direction of growth.

Wandering cells, which progress relatively rapidly by means of ameboid movements, abound wherever growth is taking place. We have

not seen these divide. They are especially active and abundant in regions where there is a dense growth of fibroblasts.

Fibroblasts have been observed to send out long slender processes, into which relatively highly refractile material slowly works its way. After this has continued for a period (variable), the cell rapidly assumes a spherical form; mitosis begins; the refractile material gathers in two groups, and in a great burst of agitation, during which the cell undergoes a series of distortions, it separates into two halves, each half

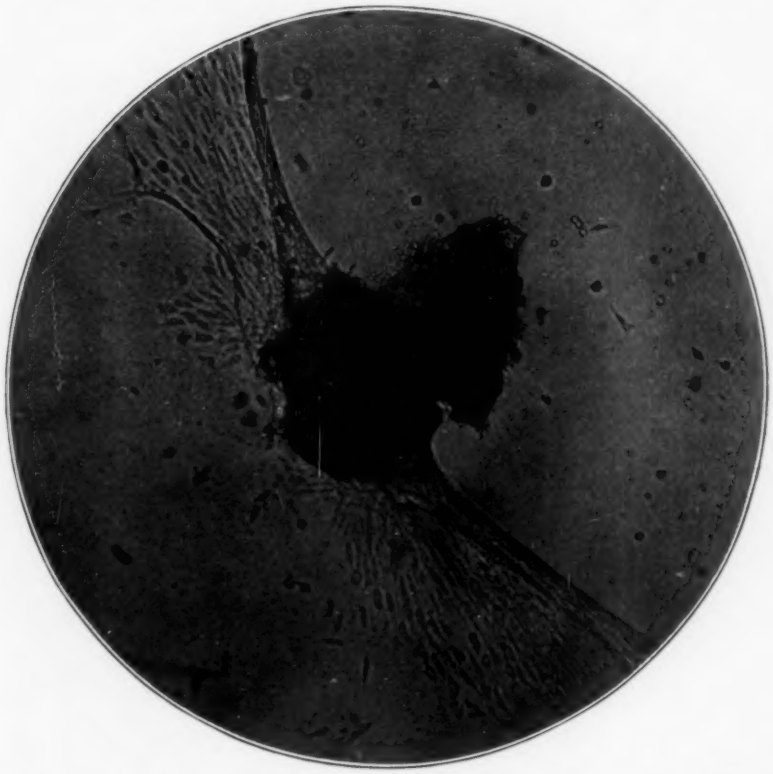

Fig. 4.—Lateral view of a culture similar to that in figure 3, with semisolid medium to the left and liquefied medium to the right. The dark strands running to the top and to the lower right are epithelium. The scattered cells are fibroblasts.

retaining its portion of the refractile substance. One of the daughter cells remains behind, while the other advances in the direction of the growth of tissue.

One important conception that the motion pictures have given us is that these cells are really constantly dynamic. Cells which appear to be at rest when observed microscopically are actually busy—now pulling, now twisting, now sending out protoplasmic processes in which

streams of granular material can be seen. Mitosis indicates pronounced activity, but even when mitosis is not in process every structure may be said to be active. The wandering cells are particularly vigorous. Division of these cells has not been seen.

In describing what we have observed in these films, we wish it to be understood that no claim to originality is made so far as photographing of the details of cell division is concerned. This has been done by several observers, notably by the late R. G. Canti, of London, England, in the

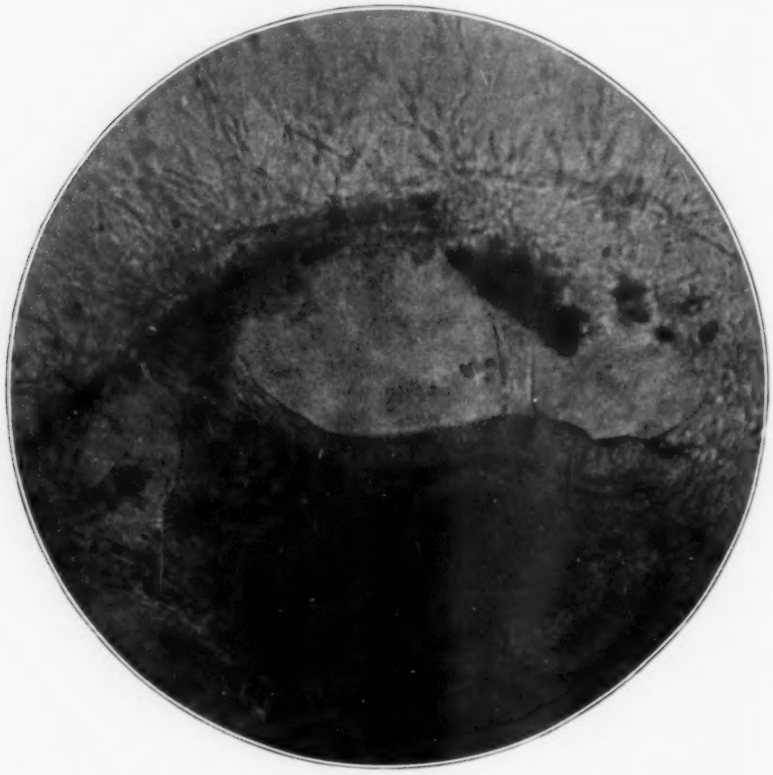

Fig. 5.—The implant is seen in the lower part of the illustration. Sheets of new tissue are growing upward; a wide sheet is seen at the left and a narrower one in the right central area. The network at the top is composed of fibroblasts.

study of cancer. Of observations which apply to the growth of ciliated epithelium, however, as stated at the beginning, we have found no previous record.

Having established and stabilized a method for obtaining relatively constant and standard growth of nasal epithelium, we trust that it may serve as a foundation for a variety of experiments which will eventually lead to more rational and effective treatment of nasal disease.

IRRIGATION BY POSTERIOR SUCTION

ITS USE IN TREATMENT OF SUBACUTE AND EARLY CHRONIC POSTERIOR SINUSITIS

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AND
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The principle of displacement described by Proetz has undoubtedly added immensely to the successful diagnosis and treatment of ailments in the posterior sinuses, particularly the sphenoid sinuses.

A minor variation of this original method, namely irrigation with gentle suction, affords an additional method of diagnosis and treatment of the entire ethmoid group of cells, except those comprising the most anterior portion of the ethmoid capsule.

Proetz [1] recently, in evaluating his method, described what he has named "washing through." This is "the application of continuous suction at one nostril while a treatment solution is being poured into the other." N. Asherson [2] reported a series of cases of children successfully treated in this manner.

Over a period of three years we have used this method in the treatment of subacute residual ethmoiditis following "colds," of chronic hyperplastic conditions of the posterior ethmosphenoid sinuses associated with postnasal drip and headache and of retrobulbar conditions of sinal origin.

DESCRIPTION OF INSTRUMENTS AND TECHNIC

The nasal irrigator is made of pyrex glass and has a capacity of approximately 120 cc., or 4 ounces (113 Gm.). Its design is similar to that of the Undine irrigator, except for the tip, which has been replaced by two nozzle-like spouts that direct the solution into the patient's respective nares.

The nasal suction tip also has been reconstructed, the bulb having been reenforced during the blowing process in order to withstand

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1. Proetz, A. W.: An Evaluation of the Displacement Method with a Review of the Literature, Ann. Otol., Rhin. & Laryng. **46**:699-734 (Sept.) 1937.

2. Asherson, N.: Nasal Sinusitis in Childhood, Lancet **1**:170-171, 1937.

Fig. 1.—Patient in the supine position with the head extended and the saline solution directed into the nares.

Fig. 2.—The nasal irrigator.

unusually heavy usage. The tip has been considerably blunted to avoid any contact with the nasal septum and yet shaped sufficiently to seal off the nares during the process of suction.

After shrinkage of the nasal mucosa with an ephedrine pack, the patient lies supine, with the head well extended over the edge of the cot or table and with the chin pointing to the ceiling, as indicated in figure 1. The nasal irrigator (fig. 2) partly filled with physiologic solution of sodium chloride or buffer solution, as the case may be, is held in the hand with the index finger over the vent and the base of the flask close to the patient's chin, so that the two spouts approach a distance of approxi-

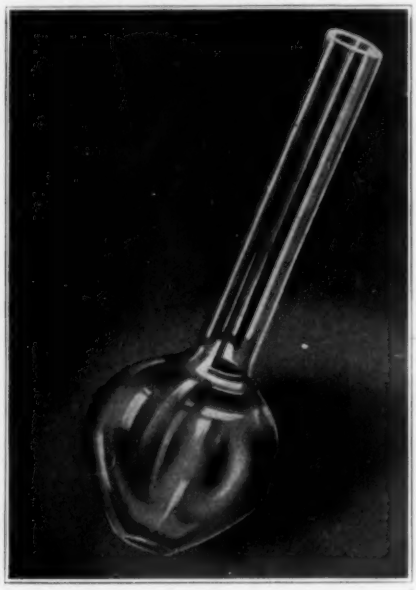

Fig. 3.—The nasal suction tip.

mately ½ inch (1.3 cm.) from the patient's external nares. This position is usually assumed when an assistant is at hand to aid the operator.

The flow of fluid into the nares of the patient is controlled by manipulating the index finger which covers the vent. When this finger is raised, the fluid flows out of the spouts into the respective nares. When the fluid level has approached the nasal orifices, the flow is arrested by covering the vent.

Gentle suction, not exceeding 3 pounds (1.3 Kg.), is then applied through the nasal tip (fig. 3). While the patient repeats the consonant "K, K, K," interrupted suction is effected by synchronously closing the other nares with the finger tip when the patient says "K" and releasing it during the interval. The process of filling the nasal cavities

with physiologic solution of sodium chloride or buffer solution and aspirating this back is continued until there is no more pus floating in the aspirated fluid. By keeping the nares filled, one exerts suction on the fluid rather than on the nasal wall.

COMMENT

Though irrigation by this method will partially fill other cells in addition to the posterior ethmoid group, we are convinced that only in the latter cells is the process carried to completion. Use of a 10 per cent solution of iodized oil in a number of cases has failed to show complete filling of the frontal, the orbital or the antral cells, though in every case a spill-over is seen. Since we previously shrink the nasal mucosa, it is our opinion that, even if filling takes place, some of the material is emptied on return of the patient to either the prone or the upright position when roentgenograms are taken, as the oil drips from the nose during this procedure.

Our results in treating the subacute conditions following one to three weeks after acute colds have been most encouraging, one irrigation frequently being sufficient to establish good drainage and the cessation of the obstructive headache which is usually present.

Irrigation of the ethmoid area one to three weeks after a cold is not likely to spread the infection, since pansinusitis is usually already present when the patient presents himself. The location of the ethmoid sinus between the frontal and the maxillary cells naturally must influence the drainage of the frontal sinus, through obstruction of its natural opening, as well as that of the maxillary antrum, through gravity or obstruction of its natural opening. Irrigation of the adjacent frontal sinuses or antrums during a period of acute ethmoiditis following a cold will almost invariably reveal some purulent material rich in organisms, a circumstance which indicates an existing diffuse infection.

It has not been uncommon in our series to have the frontal pain and tenderness disappear almost immediately after a wash, and frequently the same has been true of the pain in the maxillary sinus, so that this procedure is always resorted to by us first, before we use instruments in either of these sinuses, when an acute or subacute infection exists. We have applied this management in cases of subacute ethmofrontal sinusitis. The number of irrigations varies, of course, with the age of the sinal condition. When the condition has followed one week after a common cold, two treatments at a forty-eight hour interval usually are sufficient to accomplish a cure. When treatment has been started two weeks after the onset, four irrigations at forty-eight hour intervals, on an average, are necessary for cure. After three to four weeks of pansinusitis following a cold, six irrigations are necessary to accomplish a cure.

In 4 cases of retrobulbar neuritis due to infection of the posterior sinuses we averaged thirteen irrigations each from the date of onset to the last treatment, at which time perimetry and visual tests marked the return of the eye to its normal state.

We have found this method of equal advantage in treating the early nonallergic, chronic suppurative and hyperplastic conditions of the posterior ethmoid cells. These are the residual infections left in the posterior sinuses after neglected colds. They range in duration from months to years, and, though they do not present enough pathologic change to indicate surgical procedures, they become annoying to the patient, either because of the periodic headaches or because of the postnasal drip. These cells are so frequently the seat of chronic disease because of their location. Springing from the middle superior and supreme meatuses, they are easily isolated by swellings of the mucosa of the middle, the superior or the supreme turbinate, which prevents aeration and drainage from these areas. As Skillern [3] pointed out, they are tucked away out of the reach of the inspiratory air currents, providing an optimum condition for bacterial retention and growth. From ten to fifteen irrigations of 100 cc. given at four day intervals will usually suffice to check the annoying symptoms. In 300 cases in which this treatment has been used, the average number of irrigations given to make the patient comfortable has been twelve. Of course, this method accomplishes only a symptomatic cure.

Unfortunately, in cases of posterior infection, a fresh cold is frequently likely to cause a recurrence. It is common knowledge that patients with chronic sinusitis display an increased susceptibility to colds; hence we have been augmenting this treatment with injections of a stock vaccine made from the filtrates of 65 fresh colds. Progressing injections of this material are given after each irrigation. That our results are not attributable to vaccine therapy alone is apparent from the immediate amelioration of symptoms that we obtain. In addition, our results in a long series without vaccine therapy, as we originally carried out this treatment, are about the same as our present results. There seems to be no doubt, however, that about 25 per cent get from six to twelve months' immunity to the secondary invaders by the additional use of a vaccine.

This method of irrigation is valuable also in investigating the contents of the posterior ethmoid cells, the only group, aside from the anterior cells, that we are unable to cannulize or directly observe. One is impressed with the frequency with which material is washed up from these sinuses, though a careful examination of the nose the mucosa of

3. Skillern, R. H.: Chronic Ethmoiditis: Its Conservative Surgical Treatment, Ann. Otol., Rhin. & Laryng. **38**:716-731 (Sept.) 1929.

which has been previously shrunk fails to reveal any free material either on the meatal walls or in the nasal gutter. In doing a diagnostic irrigation, 40 to 50 cc. of solution may be washed through before material is dislodged from the cells.

With the newer knowledge of the physiology of the nasal mucosa, an objection might be raised to this method because of its effect on the mucous membrane. However, let it be remembered that the amount of negative pressure used is small, i. e., less than 3 pounds (1.3 Kg.) and that when the nose is filled to the nares the pressure is exerted for the most part on the solution.

The possibility of spreading infection to the other sinuses or through the eustachian tube to the middle ear is, of course, present. In 2,000 irrigations done on 500 patients, there have been 2 such occurrences. In neither case did the condition go on to suppuration. This accident is apparently due to swallowing during the irrigation. Since making it a practice to admonish patients against swallowing, we have had no such accidents. One must realize that this method is not applicable to refractory children, highly nervous adults or elderly persons who are unable to maintain the proper position, i. e., with the head inverted so that the chin and the external auditory canals lie in the same vertical plane, as advocated by Proetz.

RADICAL MASTOIDECTOMY

ITS USE IN TREATMENT OF DANGEROUS TYPES OF SUPPURATION OF THE TEMPORAL BONE

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PROVIDENCE, R. I.

Chronic suppuration of the temporal bone may go on indefinitely without any general systemic symptoms. The patient's only outstanding complaints may be otorrhea and impaired hearing. The otorrhea may be constant or intermittent, profuse or scanty, odorless or offensive. The impairment of hearing may be of the conductive or of the perceptive type or a combination of both.

There are two types of otitic suppuration: (*a*) the nondangerous and (*b*) the dangerous.

(*a*) Nondangerous suppuration involves invariably the mucous membrane of the eustachian tube and the middle ear and occasionally the epitympanic region.

(*b*) The dangerous variety not only involves the mucous membranes but attacks bony structures. In the progress of the disease, suppuration and erosions of such important vital bony structures as the cerebral and cerebellar dural plates, the lateral sinus plate, the facial canal and the bony labyrinth may occur.

Bearing in mind the dangers of chronic suppuration, I decided to review the outpatient clinical records of cases in which the diagnosis was chronic purulent otitis media for the purpose of selecting those cases which I felt required radical mastoidectomy. A personal examination was resorted to in order to select those cases in which the condition came under the category of dangerous chronic suppuration of the ear. This study was commenced in January 1935 and completed, as far as operative procedures were concerned, in December 1936.

Over 200 cases were investigated in the clinics of the Rhode Island and the Miriam Hospital in Providence, R. I., and the Memorial Hospital in Pawtucket, R. I. In 25 of these (12.5 per cent) definite indications for radical mastoidectomy were observed. One additional case,

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Thesis submitted to the faculty of the Graduate School of Medicine of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Master of Medical Science (M.Sc.[Med.]) for graduate work in otolaryngology.

to be reported later, that of a patient admitted to the Rhode Island Hospital without previous attendance in the otologic clinic, is included in the selected group.

The ages in the group ranged from 7 years to 59. The patient in 11 cases was male, and in 15, female. The duration of the aural discharge ranged from one to fifty years. In 3 cases the infection of the ear was bilateral and in 23 unilateral. Simple mastoidectomy had been done once in 3 cases and twice in 2. The infection of the ear dated back to scarlet fever in 11 cases, measles in 6, diphtheria in 1, head cold in 5 and tonsillitis in 3. Tonsillectomy and adenoidectomy had been done in 24 cases, in 5 before and in 19 after the aural infection had occurred. Submucous resection of the nasal septum had been performed in 1 case. Aural polyps had been removed repeatedly in 7 cases. As to nationality, the patient in 11 cases was American; in 5, Italian; in 3, Portuguese; in 1, Armenian; in 1, Polish; in 2, French; in 2, Jewish, and in 1, Irish.

In the study of this group of cases before operation, the following procedures were employed:

1. A complete general physical examination, including readings of the blood pressure and analysis of the urine.

2. A complete examination of the blood, including an estimation of hemoglobin, white, red and differential cell counts and a Wassermann test.

3. An examination of the aural discharge for consistency, amount, odor, presence or absence of cholesteatomatous particles and bacterial flora.

4. A study of the ear drum and middle ear for the location and size of perforations and the presence of polyps and granulation tissue.

5. A fistula test, made with a modified Politzer inflating apparatus.

6. Hearing tests of both ears.

7. Complete roentgen studies of both mastoids, including the petrous pyramids.

This study deals only with cases selected because of long-standing infection, including such pathologic conditions as chronic infection of the bone, cholesteatoma, symptoms of beginning or existing intracranial extension and, in a few instances, persistently recurring polyps. Infection of the middle ear in which the pathologic change was essentially in the eustachian tube was not included. In none of the cases had the condition responded to conservative treatment, which had been carried out under various physicians over the course of years of attendance at the clinics. The measures which had been employed included: tonsillectomy and adenoidectomy; local nasal treatment and intranasal opera-

tions on the nasal accessory sinuses; treatment of the nasopharynx; removal of aural polyps; use of drops of alcohol, metaphen or mercurochrome; use of boric acid and iodized powders, and in a number of cases zinc ionization.

HISTORICAL SUMMARY

A cure for chronic discharge from the ears has been sought by physicians throughout the ages. It was not until the latter part of the nineteenth century that surgical principles developed which led to the present day technic of radical mastoidectomy. Küster and Von Bergmann were the leaders in the trend toward radical procedures. Küster recommended the removal of the posterior bony auditory wall and Von Bergmann the removal of the outer osseous wall of the attic. Thus all the various cavities in the temporal bone, that is, the antrum, the attic, the tympanum and the meatus, were made into one large easily drained cavity. This work was followed by modifications, the most noted being those of Jansen, Zaufal and Stacke (about 1890). Jansen suggested the removal of the posterior tympanic margin where it bridges the lower posterior portion of the tympanic cavity. Zaufal worked forward from the antrum to the attic, and Stacke operated backward from the attic to the antrum. Stacke's procedure is helpful in locating the antrum, especially when the sigmoid sinus is located close to the posterior wall of the canal (Ballance [1]).

INDICATIONS

Radical mastoidectomy is indicated in cases of the dangerous types of chronic suppuration of the temporal bone [2] which may be described as those in which there is evidence of chronic osseous disease of the mastoid and the middle ear, those in which symptoms of acute infection occur in the presence of chronic otorrhea, those in which cholesteatoma can be demonstrated, those in which unexplained paralysis of the facial nerve occurs during the course of chronic purulent otitis media, those in which there is evidence of complications in the labyrinth, the lateral sinus or the intracranial region and those in which aural polyps persistently recur.

1. Ballance, C.: Mastoid Operation: A Glimpse into Its History, Arch. Otolaryng. **16**:55 (July) 1932.

2. Curtin, J. F.: Indications for a Radical Mastoid Operation and the Technic of the Same, Journal-Lancet **55**:576 (Sept. 1) 1935. Kerrison, P. D.: Diseases of the Ear, Philadelphia, J. B. Lippincott Company, 1923, pp. 215-218. Kopetzky, S. J.: Otologic Surgery, New York, Paul B. Hoeber, Inc., 1929, p. 174. Smith, S. M.: Indications for the Radical Mastoid Operation, in Jackson, C., and Coates, G. M.: The Nose, Throat and Ear, and Their Diseases, Philadelphia, W. B. Saunders Company, 1930, p. 537.

ROENTGEN STUDIES AND ROENTGEN THERAPY

Roentgen studies of the mastoids were of great help in evaluating the degree of pathologic change, giving an objective picture of the anatomic structure of the mastoid as well as invaluable information regarding necrosis of the bone and cavitation. In nearly all cases the operative findings tallied with the results of the preliminary roentgen studies. In all cases pictures were taken of the base of the skull to show the petrous pyramids. In several cases sclerosis of a previous pneumatic petrous structure was indicated, but in none was there evidence of definite active infection.

High voltage roentgen therapy was given postoperatively in 5 cases in which the usual methods failed to retard the growth of granulations. An excellent clinical result was obtained in 4 of these cases. In the fifth case in which roentgen therapy was used there was no response, possibly because of the presence of marked general debility and questionable pulmonary tuberculosis.

BACTERIOLOGIC OBSERVATIONS

Smears and cultures of material taken from the middle ear and the mastoid showed a variety of organisms. No organisms were seen on smears or grown in cultures in 9 cases. Staphylococcus albus was reported in 4 cases, Streptococcus haemolyticus in 2, and gram-positive diplococci, not definitely identified but possibly pneumococci or streptococci, in 3. In these and the remaining cases there were various contaminations by Streptothrix, fusiform bacilli, spirilla, Bacillus proteus, Escherichia leporis, Proteus ammoniae and Bacillus coli.

As can be noted from these bacteriologic findings, a small percentage of pyogenic organisms was obtained. This is not surprising when one considers that in all cases the ears had been suppurating over long periods. The original pyogenic organisms probably had died out, become attenuated or been crowded out entirely by secondary nonpyogenic invaders.

RADICAL OPERATION

An effort was made to eradicate all the diseased bone. The facial ridge was removed as low down as possible, consistent with the safety of the facial nerve. The overhang of the epitympanic space was removed. The malleus and the incus also were removed if present. The tympanic end of the eustachian tube and the mucosa of the middle ear were curetted. The annulus tympanicus was removed and the floor of the tympanum was lowered. In 2 cases in which roentgenograms showed the lateral sinus well forward and close to the posterior wall of the canal, the operation was performed from the middle ear backward. In all other cases the mastoid antrum was entered from behind.

All postaural incisions were closed with interrupted silkworm gut sutures. Meatal flaps were made at the time of operation in all but 1 case. Panse or Körner flaps were employed. The radical cavities were packed rather firmly with iodoform gauze.

PATHOLOGIC CONDITIONS FOUND AT OPERATION

The following conditions were found at operation:

	Number of Cases
Erosion of the lateral sinus plate	2
Erosion of the dural plate	4
Erosion of the bony capsule of the horizontal semicircular canal	1
Erosion of the facial canal with the nerve exposed	1
Necrosis of the posterior bony wall of the canal	1
Extradural abscess	2
Absence of ossicles	17
Erosion of the stapes (partially attached to the oval window)	1
Portion of the incus free in the middle ear (no other ossicles found)	4
Partial necrosis of the malleus and the incus	5
Polyps in the middle ear	6
Cholesteatoma in the mastoid, the middle ear or both	18
Necrosis of bone without cholesteatoma or polyps	2

POSTOPERATIVE TREATMENT

In cases of uncomplicated disease the patient remained in the hospital an average of seventeen and a half days. Sutures were removed on the fifth day. Packings in the radical mastoidectomy cavity were removed at this time or earlier if necessary. The cavity was dry cleansed and gently repacked with plain sterile gauze. In cases in which there was considerable moisture, boric acid or iodized powder was insufflated into the cavity before the gauze dressing was inserted. During the stay in the hospital the ears were treated daily. For the following two weeks they were treated every third day. After this they were treated at weekly intervals until complete epithelization and dry cavities were obtained. During the period of postoperative care, granulations were retarded by cauterization of small areas with silver nitrate. When the granulations were exuberant, the cavity was treated with a 10 per cent solution of cocaine and curettage employed. In several cases zinc ionization was used. High voltage roentgen therapy was administered in 5 cases, according to the technic of Ersner and Weiner,[3] to inhibit the growth of granulations and to promote epithelization. In cases in which granulations grew slowly and the discharge was scant and thin, saturated solution of boric acid in alcohol was prescribed. Patients reported regularly each month for removal of cerumen and detritus.

3. Ersner, M. S., and Weiner, L. H.: Roentgenotherapy in Otorrhea Following Radical Mastoidectomy, M. Rec. **140**:588 (Dec. 5) 1934.

POSTOPERATIVE COMPLICATIONS

The following complications arose after operation:

	Number of Cases
Subdural abscess (temporal lobe) with secondary paralysis of facial nerve	1
Cerebrospinal meningitis (Str. haemolyticus)	1
Delayed paralysis of facial nerve by pressure from dressing	1

REPORT OF CASES

For purposes of publication it has been necessary to omit the detailed history of most of the cases. Only a few, in which there were particular complications and other noteworthy features, are described. The clinical résumé of the complete series of cases is reported in the summary table.

CASE 2.—V. B., an Armenian man aged 38, was admitted to the hospital on April 22, 1936. This case is mentioned because of the finding at operation of an exposed facial nerve. While a cholesteatoma which filled the whole mastoid cavity was being removed, the patient's face twitched. Examination showed the nerve exposed from the region of the antrum down toward the tip for about 2 cm.

CASE 5.—J. M., a Portuguese boy aged 13, was admitted to the hospital on April 2, 1936. This boy gave a history of recurring polyps which had been removed numerous times during the course of the infection of his ear. At operation a large polypoid mass was found to involve the mastoid, the middle ear and the external canal. The mass eroded the aditus and enlarged the antrum. Microscopic examination of the removed polyp showed the "surface covered with stratified squamous epithelium of a transitional type. The epithelium dips deeply into the underlying tissue, forming crypts. Some of the crypts are seen in cross section. Beneath the epithelium is loose connective tissue, in places so vascular that it suggests lymphoid tissue. Many of the cells are plasma cells, and a few are polymorphonuclear cells. The condition is probably only an inflammatory polyp, but it is impossible definitely to rule out lymphoma. The diagnosis, chronic inflammatory aural polyp." With no unusual procedures in the after-treatment, the cavity left by the mastoidectomy was completely epithelized and dry at the end of three months and has remained so to date.

CASE 13.—E. D., an American woman aged 22, was admitted to the hospital on Aug. 19, 1935.

History.—The patient had had a constant discharge from the right ear since the age of 9 years, when she had had diphtheria. She had had intermittent local treatments for several years, without material benefit. She had been admitted to this hospital because of increase in the discharge and severe pains in the right ear and temporal region four months before the admission here reported. Simple mastoidectomy on the right had been performed by another surgeon, and the patient had been allowed to go home at the end of three weeks. The discharge had continued to be profuse and foul, and the patient still complained of intermittent pain in the right ear. She had been readmitted to the hospital three months after the simple mastoidectomy for further observation and treatment.

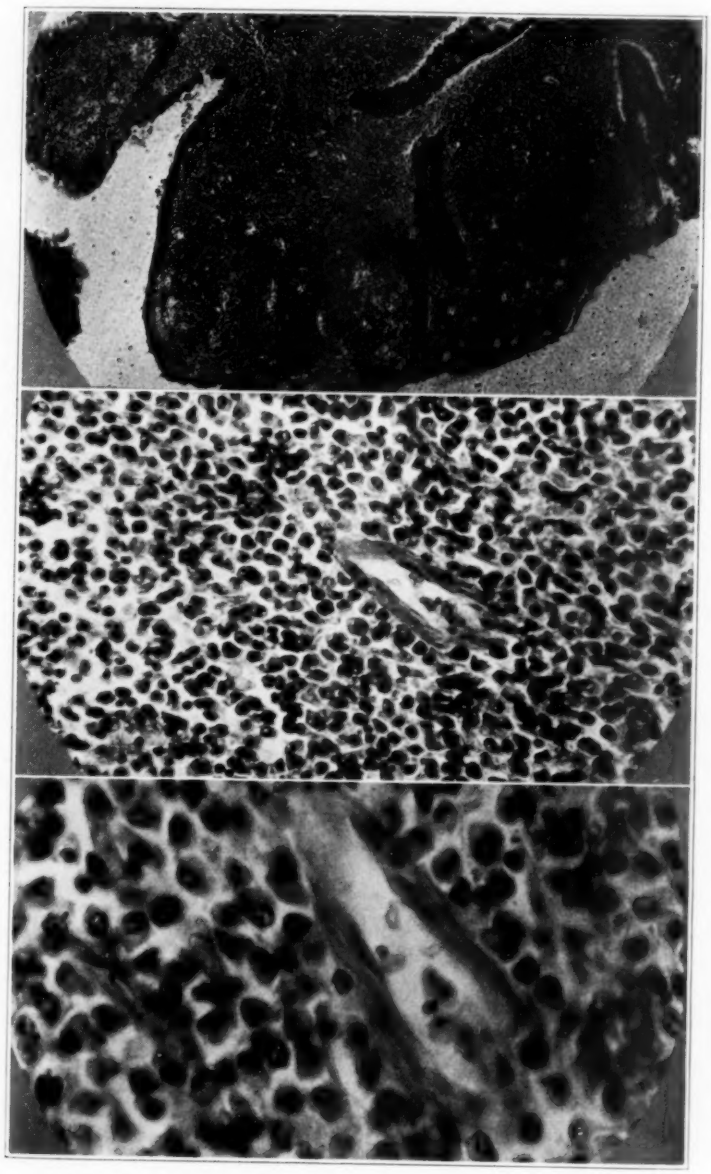

Fig. 1 (case 5).—Photomicrographs of tissue.

Summary of Twenty-Six Cases

Case and Sex	Age and Ear	Cause of Infection	Duration, Years	Previous Surgical Intervention	Preoperative Symptoms*	Operative Findings	Postoperative Complications	Postoperative Treatment	Condition of Mastoidectomy Cavity	Effect of Operation on Hearing
1 F	24 R	Scarlet fever	17	Tonsillectomy and adenoidectomy	Right temporal headache; tinnitus	Cholesteatoma; necrosis of the wall of the postauricular bony canal	None	Powders; cautery	Dry in 5 mo.	Unimproved
2 M	38 R	Head cold	15	Tonsillectomy and adenoidectomy; polypectomy	Right parietal headache	Cholesteatoma; exposed lateral sinus; exposed facial nerve	None	Powders; cautery	Dry in 3 mo.	Unimproved
3 M	18 R	Head cold	2	Tonsillectomy and adenoidectomy; polypectomy	None	Necrosis of the bone; polyp	None	Cautery; curettage	Dry in 15 mo.	Unimproved
4 M	11 L	Measles	9½	Tonsillectomy and adenoidectomy	None	Necrosis of the bone; cholesteatoma	None	Powders; cautery	Dry in 2 mo.	Improved
5 M	13 L	Measles	10	Tonsillectomy and adenoidectomy	None	Necrosis of the bone; polyp	None	Powders; cautery	Dry in 3 mo.	Unimproved
6 F	20 R	Scarlet fever	15	Tonsillectomy and adenoidectomy; polypectomy	Right temporal pain	Necrosis of the bone; polyp	None	Powders; cautery	Dry in 8 mo.	Unimproved
7 M	18 R	Measles	9	Tonsillectomy and adenoidectomy	Bloody discharge from right ear	Necrosis of the bone; cholesteatoma	None	Powders; cautery; zinc ionization; roentgen therapy	Dry in 15½ mo.	Unimproved
8 F	11 R	Scarlet fever	4	Tonsillectomy and adenoidectomy	Superimposed acute mastoiditis	Necrosis of the bone; cholesteatoma	None	Powders; cautery	Dry in 2 mo.	Improved
9 F	7½ R	Scarlet fever	5	Tonsillectomy and adenoidectomy	None	Necrosis of the bone; cholesteatoma	Measles	Powders; cautery; zinc ionization	Dry in 7 mo.	Improved
10 F	15 R	Scarlet fever	4	Tonsillectomy and adenoidectomy	None	Necrosis of the bone; cholesteatoma	None	Powders; cautery; zinc ionization; roentgen therapy	Dry in 18 mo.	Unimproved
11 F	59 R	Scarlet fever	50	None	Dizzy spells; vomiting; tinnitus	Necrosis of the bone	None	Powders; cautery	Dry in 8 mo.	Unimproved
12 M	12 R	Head cold	8	Tonsillectomy and adenoidectomy	None	Necrosis of the bone; cholesteatoma; erosion of the tegmen antri	None	Powders; cautery; zinc ionization	Dry in 6 mo.	Unimproved
13 F	22 R	Diphtheria	13	Tonsillectomy and adenoidectomy; simple mastoidectomy	None	Necrosis of the bone; cholesteatoma	General debility; "rheumatic heart"; pulmonary tuberculosis	Powders; cautery; zinc ionization; roentgen therapy	Dry for 2 mo.; moist since then	Worse

14 F	15 R	Scarlet fever and measles	1	Tonsillectomy and adenoidectomy; polypectomy	None	Necrosis of the bone; cholesteatoma; polyp	Diffuse meningitis; septicemia (Str. haemolyticus)	None	Patient died	No postoperative hearing tests
15 M	37 L	Head cold	20	None	Mastoid pain; vertigo; vomiting; facial weakness	Extradural abscess	Abscess of the temporal lobe of the brain	Alcohol and boric acid	Moist	Worse
16 M	31 R	Tonsillitis	3	Tonsillectomy and adenoidectomy; submucous resection of the septum	Right hemicrania; slight vertigo	Necrosis of the bone; cholesteatoma	None	Powders; cautery	Dry in 2 mo.	Unimproved
17 M	40 R	Head cold	5	Tonsillectomy and adenoidectomy; simple mastoidectomy twice	Postauricular sinus; superimposed acute mastoid infection	Necrosis of the bone; cholesteatoma	None	Powders; cautery	Dry in 2½ mo.	Improved
18 F	30 L	Measles	27	Tonsillectomy and adenoidectomy; right simple mastoidectomy	Left temporal headache; slight vertigo	Necrosis of the bone; cholesteatoma	None	Powders; cautery; roentgen therapy	Dry in 18 mo.	Unimproved
19 F	30 L	Scarlet fever	20	Tonsillectomy and adenoidectomy; left simple mastoidectomy	Left temporal headache; pain in the left mastoid	Necrosis of the bone; cholesteatoma; erosion of the dural plate	Acute mastoiditis on the right side	Powders; cautery; zinc ionization	Moist	Worse
20 F	10 L	Tonsillitis	9	Tonsillectomy and adenoidectomy; polypectomy	None	Necrosis of the bone; polyp	None	Powders; cautery; curettage	Dry in 6 mo.	Improved
21 F	19 L	Tonsillitis	4	Tonsillectomy and adenoidectomy; polypectomy	Pain in the mastoid	Necrosis of the bone; erosion of the dural plate; polyp	Rubella	Powders; cautery	Dry in 2 mo.	Improved
22 F	14 L	Measles	12	Tonsillectomy and adenoidectomy	Pain in the mastoid	Necrosis of the bone; cholesteatoma	None	Powders; cautery	Dry in 7 wk.	Improved
23 M	25 L	Measles	20	Tonsillectomy and adenoidectomy	Left temporal headache; slight vertigo	Necrosis of the bone; cholesteatoma	None	Powders; cautery; roentgen therapy	Dry in 14 mo.	Unimproved
24 M	10 R	Scarlet fever	6	Tonsillectomy and adenoidectomy	Right temporal headache; mastoid pain	Extradural abscess	Paralysis of the right facial nerve	Powders; cautery	Dry in 3 mo.	Improved
25 F	26 L	Head cold	7	Tonsillectomy and adenoidectomy; left simple mastoidectomy	Left temporal headache; vertigo; nausea; vomiting	Necrosis of the bone; cholesteatoma	None	Powders; cautery	Dry in 3 mo.	Unimproved
26 F	30 L	Scarlet fever	25	Tonsillectomy and adenoidectomy; left simple mastoidectomy twice	Left temporal headache; vertigo; ankylosis of the left mandibular joint	Necrosis of the bone; erosion of the tegmen antri; erosion of the lateral sinus plate; erosion of the lateral horizontal semicircular canal	None	Powders; cautery	Dry in 9 wk.	Unimproved

* Otorrhea and deafness were among the preoperative symptoms in all cases.

Otoscopic Examination.—There was a large posterior perforation of the right ear drum, with polypoid tissue in the middle ear. The discharge was profuse thick greenish yellow pus, with a foul odor.

Roentgen Examination.—The defect of the previous operation on the right mastoid was present. The petrous pyramid was slightly cellular but not decalcified.

Laboratory Observations.—The Wassermann reaction of the blood was negative. The erythrocyte count was 4,370,000, with 86 per cent hemoglobin; the leukocyte count was 10,600. The blood smear and the urine were normal. No organisms were obtained from cultures or smears of material from the right ear.

Operation.—On August 24, at operation, the old mastoidectomy cavity on the right was found to be filled with fibrous and osseous tissue. The periantral area was necrotic. A small portion of the head of the malleus was found. The other ossicles were missing. The middle ear was filled with cholesteatomatous material and polypoid mucous membrane.

Progress.—The patient was discharged from the hospital on the tenth day after the radical mastoidectomy. The ear was given the usual postoperative treatment, and the cavity left by the mastoidectomy was dry at the end of four months. Two months later the patient was readmitted to the hospital, and complete hysterectomy was performed. During her stay in the hospital the right ear began to discharge again and has remained moist up to the time of this report. Every measure has been tried to dry the cavity, but without success. The cavity seems to have a boggy, grayish lining that pours out an exudate. Zinc ionization was used, as was high voltage roentgen therapy during a period when granulations were present. The patient has a "rheumatic heart" and is under observation for pulmonary tuberculosis. In view of the fact that the cavity left by the mastoidectomy had progressed toward healing and had remained dry for two months, it is fair to assume that the patient's general debilitated condition is the cause of the persistence of her moist ear. The hearing is worse than before operation.

Case 14.—E. P., an American girl aged 15, was admitted to the hospital on May 16, 1935.

History.—The patient had had continuous aural discharge on the right for one year following measles and scarlet fever. She complained of intermittent earache. One month before admission to the hospital, tonsillectomy had been done, and a large polyp had been removed from the right ear.

Otoscopic Examination.—The right ear drum showed a large posterior perforation with a protruding polyp. The discharge was dark brown and thin and had a foul odor.

Roentgen Examination.—The right mastoid showed indistinct small cells, with evidence of destruction of bone above and behind the bony meatus. No definite infection was seen in the petrous pyramids.

Laboratory Observations.—The Wassermann reaction of the blood was negative. The erythrocyte count was 4,600,000, with 85 per cent hemoglobin. The leukocyte count was 9,000. The blood smear and the urine were normal. Smear and culture of material from the right ear showed Str. haemolyticus.

Operation.—On May 21, at operation, a moderate-sized cavity filled with a cholesteatomatous mass was found above and behind the right mastoid antrum. The middle ear was filled with degenerated mucous membrane, cholesteatomatous material and a polypoid mass. Necrotic portions of the malleus and the incus were found unattached in the middle ear. The stapes was not seen.

Progress.—The immediate postoperative reaction was good. Forty-eight hours after operation, the patient had a sudden rise in temperature, from 99 to 102.2 F., and vomited several times. During the same evening the temperature rose to 103.4 F., and the patient showed slight nuchal rigidity and a suggestive Kernig sign. A lumbar puncture was done with the patient in the lateral position. The initial pressure was 200 mm. (water) and the final pressure 100 mm.; the protein content was 28 mg. and the sugar content 50 mg. per hundred cubic centimeters; there were 917 polymorphonuclears per cubic millimeter and no organisms. Lumbar puncture on the second day showed an initial pressure of 190 mm. and a final pressure of 100 mm.; the fluid contained 1,000 polymorphonuclears per cubic millimeter; Str. haemolyticus was grown on culture. On the third day a lumbar puncture showed the initial pressure of the spinal fluid to be 750 mm. and the final pressure 160 mm.; there were 718 leukocytes per cubic millimeter, with 90 per cent polymorphonuclears, and 114 erythrocytes per cubic millimeter. Str. haemolyticus was grown again on culture. No organisms were seen on smear. Typical neurologic signs of cerebrospinal meningitis were present. No hearing tests could be made after operation. Death occurred seven days postoperatively.

Postmortem Examination.—Gross examination showed no erosion of the bone surrounding the mastoidectomy cavity on the right. The petrous portion of the right temporal bone showed no evidence of infection. The lateral and sigmoid sinuses were patent, and the intima was smooth. At the base of the brain and over the cerebrum the pia-arachnoid was covered with a thin exudate of gray friable material. A large amount of cloudy fluid was present in the base of the skull after removal of the brain. The spinal cord showed the pia-arachnoid covered with a thin gray exudate, through which prominent blood vessels were visible. Beneath the dura was a small amount of gray, cloudy fluid. The lungs showed bronchopneumonia. Cultures taken from the blood grew Str. haemolyticus.

Gross and microscopic postmortem examination showed no evidence of direct extension of the infection from the right mastoid cavity to the meninges. The meningitis undoubtedly was of hematogenous origin.

Case 15.—N. L., an Italian man aged 37, was admitted to the hospital on July 29, 1936.

History.—The patient had had continuous drainage from the left ear since a head cold twenty years previously. Four days before his entrance to the hospital, he had experienced severe pain behind his left ear and felt very dizzy On admission, he suffered from vertigo, vomiting, tenderness over the left mastoid and mild weakness of the facial muscles on the same side. The eyegrounds were normal. A lumbar puncture, done with the patient in the lateral position, showed normal fluid and dynamics. The temperature was normal.

Otoscopic Examination.—The left ear drum showed a large posterosuperior perforation. There was a profuse heavy foul brownish discharge.

Roentgen Examination.—The left mastoid was sclerosed throughout, with a large area of rarefaction above and behind the bony meatus, suggesting cavitation.

Laboratory Observations.—The Wassermann reaction of the blood was negative. The erythrocyte count was 4,800,000, with 84 per cent hemoglobin; the leukocyte count was 10,000. The blood smear and the urine were normal. A culture of material from the left ear produced fusiform bacilli and unidentified gram-positive diplococci.

Operation.—On August 8, at operation, the left mastoid was found sclerotic throughout. In the upper anterior portion, above the antrum, was a large extradural abscess, from which considerable yellowish pus was evacuated. The dural

plate was found eroded over an area of approximately 1.5 cm. The dura in this region appeared indurated and covered with granulations. These were not disturbed. The radical operation was completed with the exception of formation of the meatal flap. The middle ear was packed with iodoform gauze. The cavity of the abscess was drained through the postaural incision.

Progress.—After the radical operation the patient was relieved of headache, nausea and vomiting. However, the weakness of the facial muscles which was present before operation became more pronounced. On the twelfth day postoperatively severe frontal headache with photophobia and palsy of the central facial nerve developed, but there was no vertigo or vomiting. The patient had moderate rigidity of the neck and presented a positive Kernig sign. There was no nystagmus. The retinal veins were distended. A lumbar puncture, done with the patient in the lateral position, showed fluid under pressure, with a slight increase in cell count and in protein content, but no organisms. The Tobey-Ayer test gave no evidence of occlusion of the lateral sinus. It was felt that the patient had an abscess of the brain or localized pachymeningitis.

On the thirteenth day after the radical operation the middle cranial fossa was decompressed and the brain allowed to herniate. After the decompression there were no changes in the neurologic signs. The paralysis of the facial nerve, the rigidity of the neck and the positive Kernig sign persisted. The patient's general condition appeared improved, but he complained of severe frontal headache. Daily lumbar punctures showed the spinal fluid to be cloudy under pressure and sterile, with an increase in cell count and in protein content. Thirteen days after the decompression the left temporal lobe was explored, and a large necrotic abscess of the brain was evacuated. Rubber tissue drains were inserted into the abscess cavity. Culture of the pus produced gram-negative rods (not identified). For several days the patient had a stormy convalescence. Six days after the evacuation of the abscess in the temporal lobe, the headache began to subside, and the rigidity of the neck disappeared, as did all the other signs except the palsy of the facial nerve. Another lumbar puncture showed clear fluid under normal pressure, with fewer cells and a sterile culture. Improvement continued. The palsy of the facial nerve became less marked. The eyegrounds were normal. The patient was discharged from the hospital on the fifty-seventh day after the initial radical operation. Follow-up of the patient showed him to be in good general health. The paralysis of the facial nerve cleared entirely after three months. The visual fields are normal at the time of this report. The ear continues to discharge slightly, without odor. The left ear is entirely deaf, but hearing in the right ear is normal. The patient has been allowed to return to his work as a chauffeur. At this writing, fourteen months after discharge from the hospital, he has had no untoward symptoms as the result of the infection of his brain. His hearing is worse than before operation.

Case 21.—E. S., a Portuguese girl aged 19, was admitted to the hospital on April 13, 1936. There had been a spontaneous rupture of the left ear drum four years before admission, after an attack of acute tonsillitis. The discharge had been continuous ever since, at times watery and at times thick and purulent. Large rapidly recurring aural polyps had been removed six times within the preceding two years. Deafness in the left ear was progressive. Occasionally, the patient had experienced severe pain deep in the left ear. Tonsillectomy had been performed when she was 13. The left ear drum presented a large posterior perforation and a smaller perforation in Shrapnell's membrane. A large polyp protruded through the posterior perforation. There was roentgen evidence that the

left mastoid was small and noncellular and the suggestion of a small area of cavitation above the bony meatus. At operation the mastoid was found to be small, without cellular bone. There was a small area of necrosis above the bony meatus, with erosion of the dural plate in this area. Polypoid tissue was found attached to the dura and extending into the middle ear. The malleus and the incus were necrotic, and the stapes was found intact. The cavity left by the mastoidectomy was completely epithelized and dry in two months. This patient showed a 50 per cent loss of hearing before operation and only a 10 per cent loss one year postoperatively.

Case 23.—T. P., an American man aged 25, was admitted to the hospital on Feb. 20, 1936. A history of drainage from the left ear for twenty years, follow-

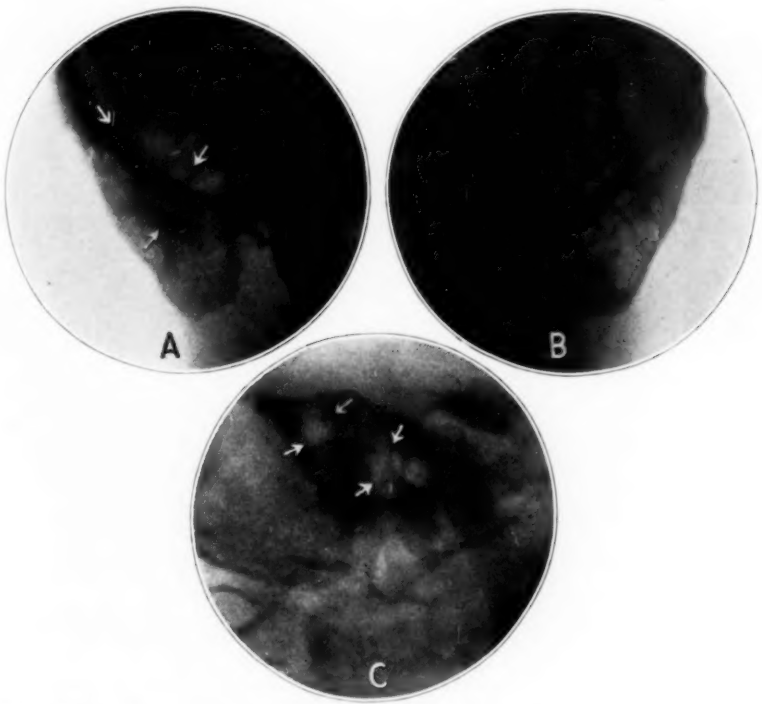

Fig. 2 (case 23).—*A*, sclerotic right mastoid with large cavitation; *B*, normal pneumatic left mastoid; *C*, sclerotic right mastoid, showing an area of necrosis posterior to the bony canal and a cavity in the posterosuperior angle.

ing measles, was obtained. For four months before admission the discharge had been increasing and had become foul. The patient complained of boring pain in the left ear, temporal headache on the left and dizziness. Operation bore out the roentgen finding of an irregular area of cavitation behind the bony canal and of a large oval cavity in the posterosuperior region of the mastoid. Cholesteatomas were found in both cavities.

Case 24.—J. K., an American boy aged 10 years, was admitted to the hospital on July 22, 1935. There was a history of discharge from the right ear for six

years, following scarlet fever. Two months before admission a large postaural abscess had developed on the right side. The abscess subsided spontaneously by drainage through the external auditory canal, without medical attention. However, the patient continued to complain of pain in the right ear and severe headache just above the auricle. At operation a large extradural abscess was uncovered. Considerable yellowish pus escaped. The radical operation was postponed until the extradural abscess had subsided. Radical operation was done twenty-three days later. The right middle ear was filled with granulations, polyps and cholesteatomatous material. Eighteen hours postoperatively, paralysis of the right facial nerve developed. The dressings on the ear were immediately removed, and within ten hours ability to move the eyelids returned. The paralysis improved, and there was complete recovery at the end of six weeks. The paralysis undoubtedly was caused by pressure.

CASE 26.—J. R., an American woman aged 30, was admitted to the hospital on July 18, 1935. Simple mastoidectomy had been performed on the left after scarlet fever when the patient was 5 years old. Measles at the age of 7 years had caused fresh involvement of the same ear, with intermittent discharge for nineteen years. Four years before admission, an infection of a sinus had started a more profuse discharge and a postaural abscess on the left side. At that time another simple mastoidectomy had been done. Since the second simple mastoidectomy, the patient had had three postaural abscesses incised; relief had ensued, but the ear continued to drain. About two weeks before admission, after swimming, the patient experienced a further increase of the dicharge from the left ear, severe earache, headache over the temple, dizziness and some ankylosis of the left mandibular joint. At operation considerable necrotic bone was found in the left zygomatic process. A moderate-sized cholesteatomatous cavity extended along the dural plate and backward behind the lateral sinus. Erosion of the tegmen antri and the lateral sinus plate was found. The bony horizontal semicircular canal was eroded. No ossicles were present. For about four days postoperatively the patient had considerable dizziness. There was no rise in temperature. Ankylosis of the jaw, headache and pain in the left ear were relieved. After nine weeks complete epithelization was obtained, and the ear was dry.

HEARING

In the preoperative investigation of this series of cases, hearing tests were made by means of the whispered and the spoken voice, tuning forks and the audiometer. The same procedures were followed postoperatively for comparison. The final results for hearing are reported as of one year following the radical operation.

The Coyne audiometer was employed. This device is electrically controlled, with seven evenly graded steps—0-64, 0-128, 0-256, 0-512, 0-1024, 0-2048 and 0-4096. The oscillations of tone and pitch from 0 to 4096 per second are controlled through an A switch and to 8192 through a B switch in such a manner as to allow the production and holding of any one of the foregoing oscillations while controlling the volume of intensity. Oscillations may be produced up to the range of audibility and down to 0, so that various tones cannot be heard. The control of intensity for each tone is always constant and can be accurately charted.

Hartmann tuning forks were used in testing bone and air conduction. The vibrations in the 512 fork lasted a maximum of ninety seconds by air conduction. Care was taken not to produce overtones. When the patient's hearing acuity was being tested before and after operation, a damper, such as Bárány's noise apparatus, was employed to exclude borrowed audibility from the good ear in tests of the diseased ear.

The accompanying audiograms (figs. 3-5) have been selected to illustrate the result of operation in 1 case each of improved, unimproved and worse postoperative hearing. Hearing was improved in 8 cases (32 per cent), unchanged in 14 cases (56 per cent) and worse in 3 cases (12 per cent). When the percentage of change in hearing shown by the

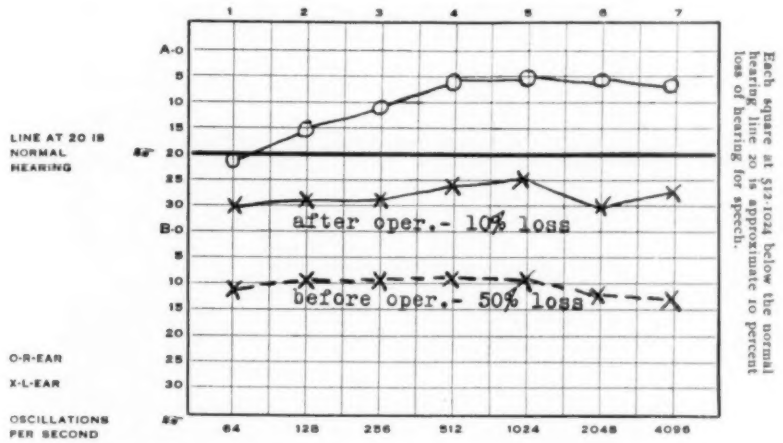

Fig. 3 (case 21).—Audiogram made of the left ear before and one year after operation. The hearing was improved. The results of preoperative and postoperative hearing tests were as follows:

	Preoperative	Postoperative (1 yr.)
Whispered voice	not heard	5 feet (152.4 cm.)
Spoken voice	20 feet (609.6 cm.)	20 feet (609.6 cm.)
Low tones	lost	no loss
High tones	no loss	no loss
Weber's test	lateral, to left	slight lateral, to left
Schwabach's test	30 seconds	35 seconds
Rinne's test—air	none	63 seconds
—bone	30 seconds	35 seconds
Audiometer	50% loss of hearing	10% loss of hearing
Diagnosis:	Deafness of conductive type	

tests was so slight that there was no material practical benefit or detriment to the patient, the case was classified as one of unchanged hearing.

The results of hearing tests in 25 cases are given. In 1 case the patient died, and therefore no final hearing tests could be obtained for

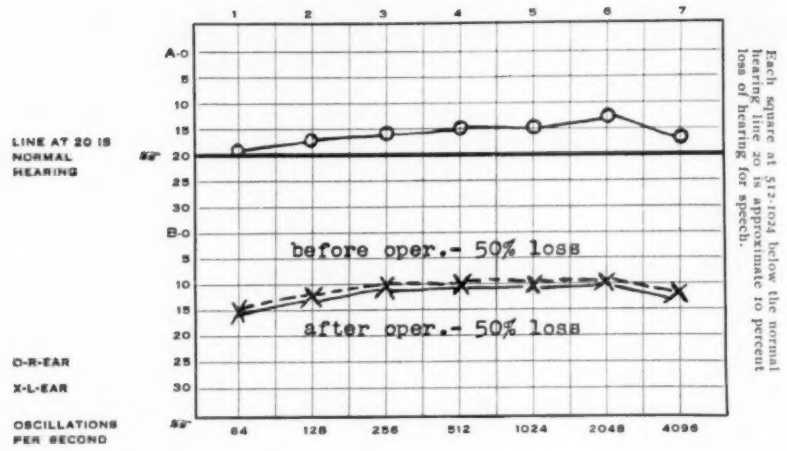

Fig. 4 (case 23).—Audiogram made of the left ear before and one year after operation. The hearing was unimproved. The results of preoperative and postoperative hearing tests were as follows:

	Preoperative	Postoperative (1 yr.)
Whispered voice	not heard	6 feet (183 cm.)
Spoken voice	not heard	6 feet (183 cm.)
Low tones	lost	lost
High tones	diminished	diminished
Weber's test	lateral, to left	lateral, to left
Schwabach's test	18 seconds	18 seconds
Rinne's test—air	none	none
—bone	18 seconds	35 seconds
Audiometer	50% loss of hearing	50% loss of hearing
Diagnosis:	Deafness, of combined conductive and perceptive types	

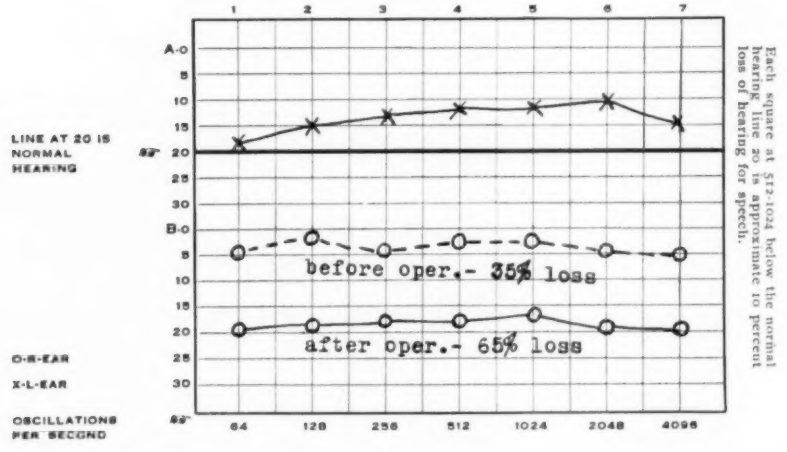

Fig. 5 (case 13).—Audiogram made of the right ear before and one year after operation. The hearing was worse. The results of preoperative and postoperative hearing tests were as follows:

	Preoperative	Postoperative (1 yr.)
Whispered voice	not heard	not heard
Spoken voice	10 feet (304.8 cm.)	2 feet (61 cm.)
Low tones	diminished	diminished
High tones	lost	lost
Weber's test	lateral, to left	lateral, to left
Schwabach's test	15 seconds	4 seconds
Rinne's test—air	none	none
—bone	15 seconds	4 seconds
Audiometer	35% loss of hearing	65% loss of hearing
Diagnosis:	Deafness, of perceptive type	

comparison. Among the 8 cases of improved hearing, the age in 7 was between 7 and 9 years and in 1, 40. In this group, the improvement in hearing varied from 10 per cent to 40 per cent. In case 21 operation was performed because of persistently recurring polyps. The stapes was found intact in the oval window and showed no pathologic involvement. In this case there was 50 per cent loss of hearing in the diseased ear before operation and only 10 per cent loss one year after radical mastoidectomy. The improved hearing in the other cases undoubtedly resulted from good receptive power in the cochlea and diligent postoperative care to prevent heavy granulations from accumulating in the region of the posterior tympanic wall. The development of a thin epidermal layer over the promontory permits better reception of sound. This observation is in keeping with the recent work of Hughson,[4] who demonstrated the benefits of grafts to the round window in certain types of deafness.

In 4 cases of total deafness before operation the condition is reported as unchanged.

Of the 3 cases of diminished hearing after the radical operation, in 1 there was abscess of the temporal lobe of the brain which necessitated extensive surgical intervention. In the other 2 there was a perceptive type of deafness, and operative improvement was not expected.

SUMMARY AND RECAPITULATION

Twenty-six cases were selected for radical mastoidectomy because of the presence of definite indications which have been enumerated. Each case was submitted to careful preliminary investigation, including physical examination, blood tests, bacteriologic examinations, hearing tests and roentgen studies.

Investigation of the antecedent history of the chronic mastoid infections revealed the condition to have followed measles in 6 cases, scarlet fever in 10 and a combined infection of measles and scarlet fever in 1.

The shortest period of hospitalization after radical operation was seven days. The longest was fifty-seven days. The average stay in the hospital after radical operation in all cases was sixteen days.

In 25 cases the patient is alive. In 1 case death followed septicemia caused by Str. haemolyticus and diffuse meningitis, the meningeal infection apparently occurring by way of the blood stream.

Of the complications abscess of the temporal lobe of the brain was treated successfully in 1 case. No untoward clinical symptoms have developed during the fourteen months since discharge from the hospital. In this same case paralyses of the facial nerve cleared entirely after

4. Hughson, W. D.: Grafts in the Round Window in the Treatment of Certain Types of Deafness, Arch. Otolaryng. **25**:623 (June) 1937.

treatment of the abscess of the brain. In another case, paralysis of the facial nerve caused by pressure from a postoperative dressing in the ear cleared spontaneously.

Radical operation relieved symptoms of headache in relation to the affected ear, pain in the ear itself and dizziness. In addition, the labyrinthine symptoms were relieved in 1 case in which there was a fistula of the horizontal semicircular canal.

In 8 cases (32 per cent) hearing was improved after operation; in 14 (56 per cent) hearing was unimproved, and in 3 (12 per cent) the operation made the hearing worse.

In 21 cases (84 per cent) the radical mastoidectomy cavities are dry; in 4 (16 per cent) the ears are still moist.

CONCLUSIONS

When there is evidence of chronic suppuration of the temporal bone which may produce complications potentially and seriously endangering the life of a patient, the eradication of such disease is of prime importance. The radical mastoidectomy, therefore, is indicated in those selected cases in which there are pathologic changes that may lead to dangerous intracranial extension of infection.

In all cases suppurative otitis media is accompanied with more or less impairment of hearing. Depending on the extent of involvement of the structures of the middle ear and on the degree to which the cochlea has been affected, the hearing may improve, become worse or remain unchanged after the radical operation. The impairment of hearing and, in some cases, the intracranial complications might be minimized or avoided by proper medical attention and timely surgical intervention in the acute stages of infection of the ear.

It is important to bear in mind that nondangerous types of chronic suppuration of the temporal bone at any time may become dangerous by ingrowth of epithelium forming cholesteatoma, bony involvement and extension to vital intracranial structures.

PROCESS OF HEALING IN INJURIES TO CAPSULE OF LABYRINTH

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Knowledge of the manner in which healing proceeds in clean perforating injuries of the labyrinth, such as fractures or surgical procedures, is limited. This limitation is in large part due to the paucity of histopathologic material available for study, both of the human and of the experimental animal, and to the complicating element of infection, which is so often superimposed on the initial injury.

In 1926 Ulrich [1] summarized the histopathologic material reported to date and, with his 2 cases, showed that but 18 specimens of the human temporal bone were extant in which a sufficient time had elapsed between injury and death to permit observation of the process of healing. Since that time but a few more specimens have become available for study.[2] In general the study of the available human material shows that in the first eleven days no evidence of healing can be made out; a fibrous tissue union was to be seen after three weeks, and in 2 specimens new bone formation was present at four weeks. However, no complete bony union occurred, since even after many years fibrous tissue was found in various parts of the labyrinth uniting the fragments. This has helped to explain the important clinical observation that an acute infection in the middle ear as long as sixteen years after a fracture of the labyrinth has occurred may result rapidly in fatal meningitis.[2b] In the study of the temporal bones of persons who have had such a condition, infection can be seen to spread along the connective tissue and the blood vessels, filling the fracture extending from the middle ear into the labyrinth. The consequent infection of the labyrinth then spreads to the subarachnoid space. Many otologists studying these specimens of fractured labyrinths have taken cognizance of the differences in the osteogenic properties of the different layers of the otic capsule; also, many questions have been raised, such as whether the mucous membrane of the middle ear is pinched into the site of the fracture and thus prevents bony union and whether a fracture of the labyrinth can heal so completely as to leave

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1. Ulrich, K.: Acta oto-laryng., 1926, supp. 6, p. 1.

2. (*a*) Hallpike: J. Laryng. & Otol. **52**:661 (Oct.) 1937. (*b*) Shittler, E.: Acta oto-laryng. **24**:216, 1937.

3. Footnote deleted.

no trace that could be detected in a histologic study. The great variations in time as well as in the extent of the injury and the presence of superimposed infection have limited the value of the observations on this material and the conclusions drawn from them, while experimental studies have been chiefly concerned with changes immediately after injury.

A clear understanding of the way in which various parts of the bone and soft tissues of the capsule of the labyrinth respond to direct mechanical injury is necessary. This knowledge is important not only for an understanding of cases of fractured labyrinth, but as a building stone in the foundation on which any growth of labyrinthine surgery must rest. The chief factors concerned lie in the field of osseous repair, which has received a great deal of study in connection with long bones. The special conditions prevailing in the otic and periotic structures prevent the unrestricted transposition of the results of such studies to the ear. Four distinct types of bone appear to enter into the formation of the capsule of the labyrinth: 1. The periosteal layer, which is formed from the innermost layer, or cambium, of the periosteum or perichondrium surrounding the cartilage capsule. This is the same as is formed in long bones. 2. The endochondral layer, which is formed around cartilage islands by replacing the cartilage capsule excavated by osteogenic buds. This bone is called primary endochondral bone and remains as such throughout life in the otic capsule, in contrast to the corresponding bone in other areas of the body, which is later removed and replaced by haversian bone.[4] 3. Islands of calcified cartilage, consisting of a matrix of calcified cartilage with lacunas filled with bone cells. These remain throughout life. This type of bone is striking in the human and the monkey labyrinth but is also present in the otic capsule of the cat, the dog and the rabbit. 4. The innermost layer of bone adjacent to the labyrinthine spaces, which is called the endosteal layer and is formed in membrane.

While the capsule of the labyrinth ossifies from a number of centers, their subsequent fusion is so complete that no differentiation of these centers is possible after ossification has been completed, and consequently the capsule may be considered as one bone. Ossification of the inner layers in any part of the capsule does not occur until that portion of the labyrinth has attained its maximum size, and the maximum size is attained before birth.[5] The striking absence of growth in the capsule

4. Bast, T. H.: Ossification of the Otic Capsule in Human Fetuses, Publication 121, Carnegie Institution of Washington, 1930; Contrib. Embryol. **21**:53, 1930.

5. Bast, T. H.: Development of the Otic Capsule: Resorption of Cartilage in the Canal Portion of the Otic Capsule in Human Fetuses and Its Relation to the Growth of Semicircular Canals, Arch. Otolaryng. **16**:19 (July) 1932.

of the labyrinth after birth is in marked contrast with the nature of the other bones in the body and is reflected in a practically fixed state of the bone of the capsule, particularly the endochondral and endosteal layers as well as the islands of calcified cartilage. Furthermore, the blood supply of the bone of the capsule is distinct from that of the structures within the labyrinth, and no anastomosis between the two is normally present. The early mature development of the cochlea in the experimental animals, such as the dog or the rabbit, as well as the architecture of the capsule of the labyrinth and the nature of its blood supply closely resembles the conditions found in man. Thus observations on these experimental animals can give valuable information with respect to the reaction of these structures to injury.

For these reasons it appears indicated to report observations on experimental animals (rabbits and dogs) on the labyrinths of which various types of lesions were produced, perforating and nonperforating, under sterile precautions. The operation consisted of incising the neck, exposing the under surface of the bulla and making a small hole in the bulla, thus exposing the cochlear capsule. Various types of lesion were made in the cochlear capsule. Many of the animals were used in a study of the effect of perforating injuries on cochlear function, carried on in this laboratory.[6] The animals were then killed and their temporal bones removed and prepared for sectioning in the usual manner. The serial sections of temporal bones from 52 animals were examined, including 11 removed within a few hours after operation and 5 that showed infection. All the dogs were young, but their exact age was unknown. The rabbits were all about 6 months old. In 4 dogs the periosteum over the promontory was scratched with a needle, and the animals were killed at varying times up to twenty-five days. The remaining animals were rabbits, in all but 1 of which a small perforating lesion of the cochlea was made under sterile precaution with a fine cambric needle. In the 1 exception, the injury was revealed on microscopic examination to be a nonperforating lesion penetrating about one half the thickness of the capsule. The fragility of the capsule and the technic used in making the perforating lesion resulted in small linear fractures of the bone of the capsule adjacent to the perforation. These linear fractures closely resembled the fractures of the labyrinth in man after trauma. Along with the changes in the bone of the capsule, the reaction at the site of the perforation of the bulla was observed. The histologic observations will be recorded for successive periods, with emphasis on the structures actively engaged in the process of healing.

6. Kobrak, H. G.; Lindsay, J. R.; Perlman, H. B., and Dubner, H.: Effect of Limited Cochlear Lesions on Cochlear Potentials and Middle Ear Muscle Reflexes, Arch. Otolaryng. **27**:59 (Jan.) 1938.

When one makes a small perforating injury on the cochlea of a rabbit, labyrinthine fluid is seen to escape immediately. This escape of fluid continues for a number of hours, according to the size of the injury. It is rapid when the injury is large, filling the bulla in about

Fig. 1.—Photomicrograph of the one day old cochlear injury (× 46.6), showing an entire thickness of the wall of the capsule broken off and displaced outward, with a separation in it between the periosteal layer (*A*) and the endochondral layer (*B*). *F* represents lines of fracture sealed with fibrin, *P* beginning thickening of the periosteum at the site of injury, *X* blood in the scala vestibuli and spiral ligament and *T.T.* the tensor tympani muscle.

fifteen minutes, which indicates a definite positive pressure of the fluids in the labyrinth in relation to the air pressure in the bulla.

HISTOLOGIC OBSERVATIONS

Acute Experiments (Less Than Twelve Hours).—Histologically, blood cells were seen within the spiral ligament and in the adjacent labyrinthine spaces, usually in the scala vestibuli and tympani, rarely in the scala media. The frag-

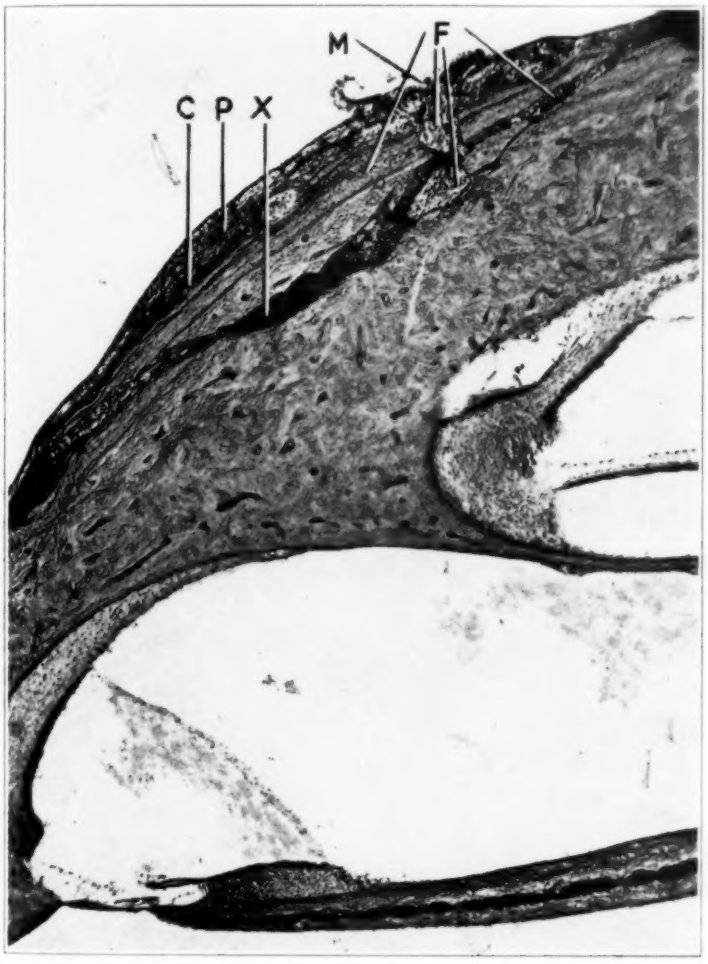

Fig. 2.—Photomicrograph (× 49) of a three day old injury of the cochlear capsule adjacent to the site of complete perforation, showing the marked thickening of the periosteum (*P*), with filling in (*F*) of the perforation and fracture lines by connective tissue proliferating from the fibrous periosteum; *C* represents the differentiation of the cambium or osteogenic layer of the periosteum, *M* the mucous membrane of the middle ear broken through and *X* blood in the depth of the fracture.

ments of bone at the site of the perforation were in part displaced outward—suggesting the effect of the flow of fluid away from the cochlea through the per-

foration. Blood cells were noted about the fragments of bone and for a short distance within and beneath the periosteal layer and within the fissures or minute linear fractures adjacent to the site of perforation.

Observations After One Day.—Blood cells were present in the same degree, and their distribution was the same as that described, but the periosteum had

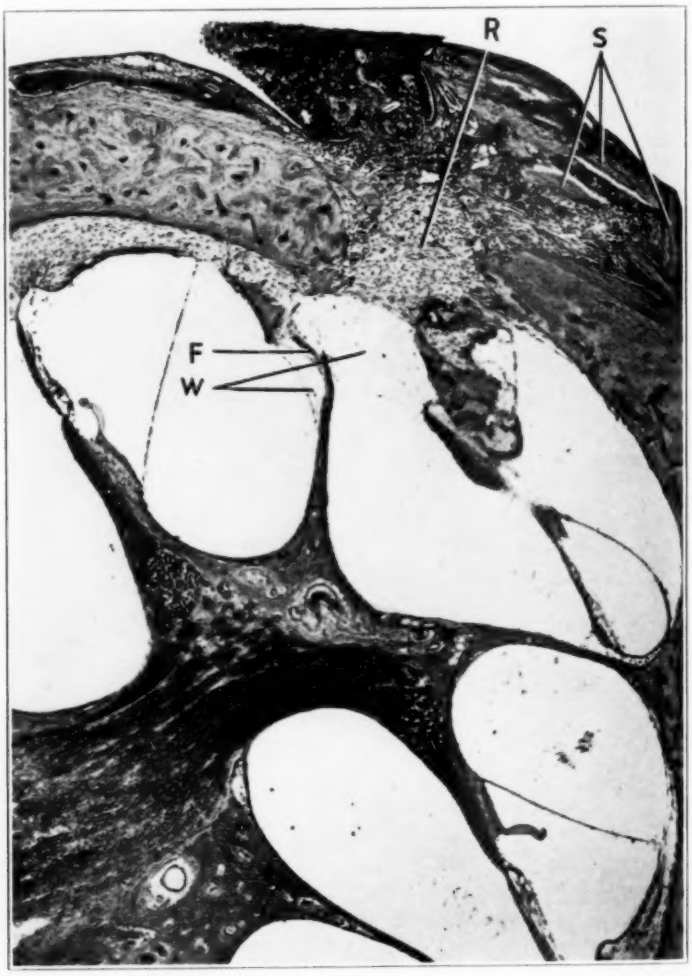

Fig. 3.—Photomicrograph of a five day old lesion of the cochlear capsule (× 48.5), showing extensive proliferation of the fibrous periosteum to surround bone spicules (*S*) and to fill the site of perforation (*R*), a fracture of the lamina between the apical and the middle coil (*F*) and a delicate meshwork of connective tissue (*W*) which probably arises from the cells covering this lamina.

become thickened. Some fibrin along with the blood cells in the lines of perforation and fracture appeared to act as the effective seal for the labyrinthine fluids (fig. 1). In 1 animal the perforating needle had stripped away the spiral ligament

from the bone of the capsule, leaving a cavity filled with blood cells and a few spicules of bone.

Observations After Three Days.—The periosteum swelled and proliferated as a growth of fibroblasts replaced the blood clot. The innermost layer, or cambium, of the periosteum became differentiated and hypertrophied and was seen to be applied to the margins of the injured and fractured capsule and to spicules of

Fig. 4.—Photomicrograph (× 66.7) of a six day old injury showing formation of new bone in the periosteal layer (*B*) against a dying bone spicule (*S*) and against old capsular bone (*E*), osteoblasts (*O*) arranged about the fragments of bone in the depth of the lesion without new bone as yet and blood (*X*) within the labyrinth.

bone in the area of the wound as a layer of cells more closely packed and with darker-staining nuclei than those of the surrounding fibroblastic tissue. The cambium is probably continuous with the haversian system and is important in

osteogenesis, since it is from this layer that callus is laid down. Blood was still present within the adjacent labyrinthine spaces and appeared essentially unchanged. There was no proliferative reaction of the endosteal layer, and no new bone was formed. Another less mature type of connective tissue could be seen adjacent to some spicules about the inner end of the perforation (fig. 2).

Fig. 5.—Photomicrograph (× 57.1) of an eight day old perforation of the cochlear capsule, showing extensive formation of new bone (*B*) against the old bone forming the wall of the perforation (*E*) and about fragments of bone (*S*). A meshwork of connective tissue is seen at the site of the fractured lamina (*F*) and blood cells at *X*.

Observations After Five Days.—Connective tissue filled the perforation and fractures throughout and extended within the labyrinth to surround fragments or spicules of bone dislodged at operation. A small number of blood cells could be seen in the adjacent perilymphatic space. The margins of the bone of the

capsule along the perforations or fractures showed no reaction. The endosteal layer showed no definite reaction. There was a definite arrangement of the connective tissue against the fractured bone and about the spicules with the inner osteogenic layer, or cambium, already well differentiated. A thin layer of bone or osteoid material could then be seen opposed to the fragment of bone and against the bone of the capusle at the margin of the perforation on the periosteal aspect (fig. 3).

Observations After Six Days.—Two of the 3 animals examined after six days had no free blood remaining within the labyrinth. One had considerable blood at the site of the operation within the labyrinth. All had formation of new bone against the spicules of bone nearest the periosteal aspect of the capsule. The

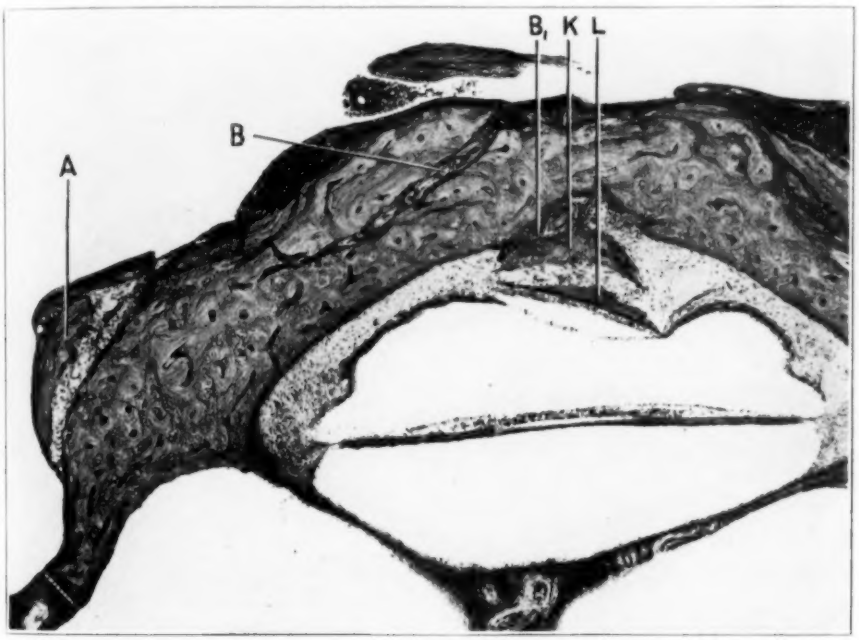

Fig. 6.—Photomicrograph (× 47.5) of a ten day lesion of the cochlear capsule adjacent to the site of perforation, showing new bone (*B*), with its nutrient vessels growing in from the periosteum in a linear fracture, chips of endosteal bone (*L*) and endochondral bone (*K*) displaced inward and one of periosteal bone (*A*) enclosed by periosteum. There is new bone (B_1) in the outer aspect of the chip of bone from the endochondral layer.

arrangement of osteoblasts with respect to the thin layer of new bone was striking. The osseous cells in some of the spicules stained poorly or not at all, indicating that the fragment was dying. Definite evidence of activity in the endosteal and endochrondal layers was lacking (fig. 4).

Observations After Eight Days.—Blood cells were present within the labyrinth at the site of the perforation. The connective tissue filling the fractures and perforation in the specimen observed after eight days contained many blood vessels. The new bone opposed to the spicules and the periosteal aspect of the

promontory and within the linear fractures was more extensive than in the six day specimen. Fragments of bone that had been completely detached from surrounding tissue showed more definite evidence of death (fig. 5). The bony lamina between the middle and the superior coil was fractured in the specimen examined, and a meshwork of delicate connective tissue was laid down in this area. This connective tissue probably arose from the thin layer of connective tissue cells which extended from the spiral ligament to cover these bony laminas. Some of the cells in this meshwork were ossified.

Observations After Ten Days.—There was little advance in the process of repair over the eight day specimen. In the specimen examined some blood was seen in the labyrinth in the scala tympani of the basal coil and none at the site of injury. The distribution of new bone with respect to the depth of the chips

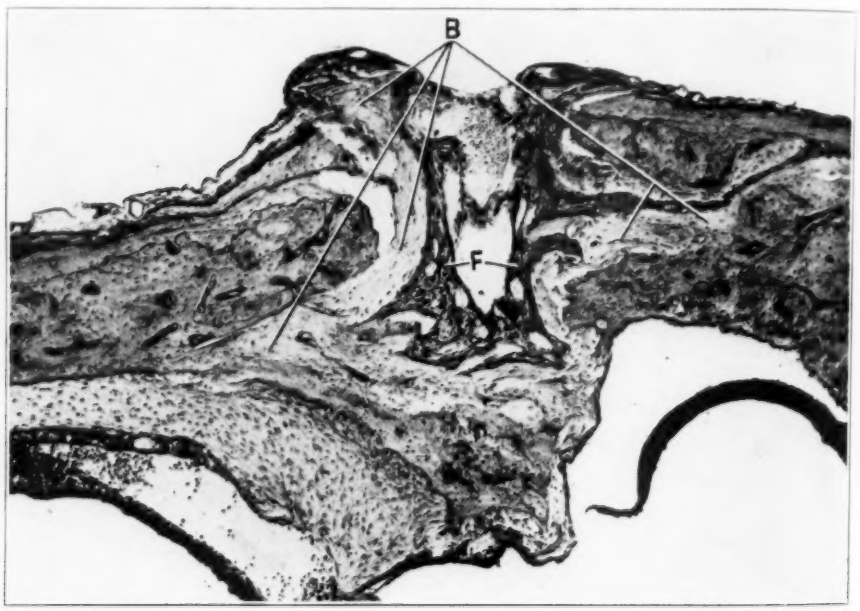

Fig. 7.—Photomicrograph (× 53.8) of a seventeen day injury of the cochlear capsule at the site of perforation, showing the extent of formation of new bone (*B*) and connective tissue (*F*) within the perforation.

of old bone in the perforation, together with the lack of evidence of activity in the endosteal and endochondral layers of the capsule, again suggested that healing was proceeding almost entirely as a result of the response of the periosteal layer. The manner in which osteogenic tissue and its vascular supply extended throughout the length of a complete linear fracture of the capsule was clearly seen.

Observations After Eleven Days.—The specimen examined after eleven days showed infection within the middle ear. The repair of the perforating injury was more advanced than in any of the previous specimens. A few pus cells within the labyrinth at the site of injury suggested the beginning invasion of the infection from the middle ear. There was a large amount of blood within the perilymphatic space.

Observations After Fourteen Days.—Of the 5 specimens examined after fourteen days, 2 showed evidence of otitis media, with invasion of the labyrinth. All were in about the same state of repair. Most of the linear fractures were completely filled with bone. The irregularity of the surfaces of the fracture due to exposure of adjacent haversian canals and lacunas resulted in an extension of the osteogenic connective tissue and resultant new bone in these areas. These

Fig. 8.—Photomicrograph (× 47.1) of a twenty-two day old perforation of the cochlear capsule, showing a wedge of new bone flaring in the periosteal and endosteal aspect and completely filling the perforation. A large viable fragment of bone (*S*) is seen in the callus. At *E* can be seen the margins of the perforation.

small outgrowths from the main callus filling the fracture produced a dovetailing between the callus and the adjacent bone of the capsule. No evidence of osteoclastic invasion of the old periosteal bone or the endochondral bone along

the line of fracture was seen. The formation of bone was more extensive, and a large callus capped the perforation, but some connective tissue remained in the perforation. Blood could still be seen within the labyrinth, with little change from the normal. Spicules surrounded by new bone were still present.

Observations After Seventeen Days.—The perforation was largely filled with bone, with a thick callus covering the site of perforation. Bundles of fibrous tissue and blood vessels could still be made out between the lamina of new bone occluding the opening in the labyrinth (fig. 7).

Observations After Eighteen Days.—The animal examined after eighteen days showed evidence of labyrinthitis in that there was a dissolution of detail of soft tissue within the labyrinth but no pus cells. The formation of considerable new bone within the labyrinth on the endosteal aspect adjacent to the site of per-

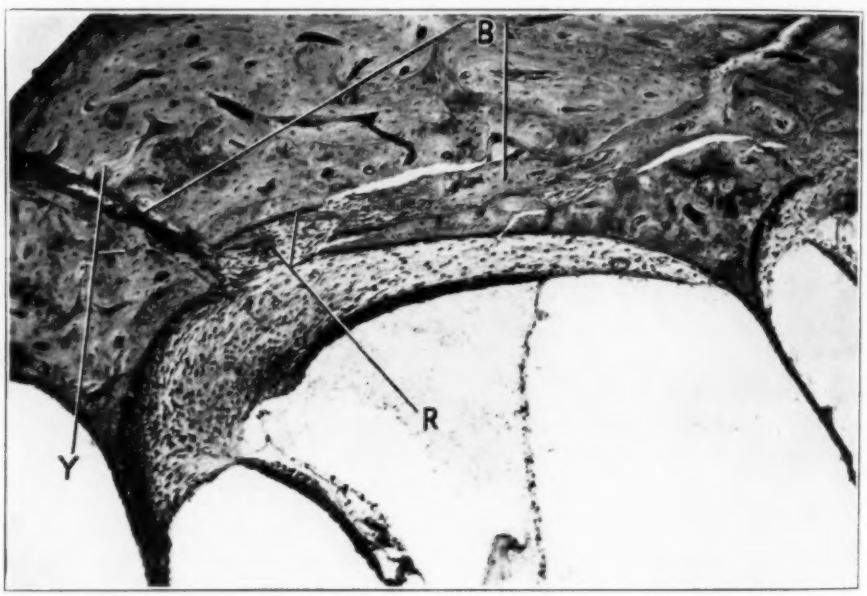

Fig. 9.—Photomicrograph (× 46.2) of another twenty-two day old injury to the labyrinth, showing the extent of formation of new bone (*B*) in the linear fractures and the dovetailing of callus and the adjacent bone of the capsule (*Y*). Note the meager osteogenic reaction of the endosteum at *R*.

foration may have been a result of the inflammatory process but was in contrast to the other specimens, without infection. Active formation of new bone and rows of osteoblasts continued at the depth of the perforation.

Observations After Twenty Days.—The perforation was well healed with bone. A fragment of bone holding the spiral ligament and pushed into the labyrinth at operation appeared viable, and new bone was laid down only on its outer aspect. The bony mass occluding the perforation was spindle shaped, flaring at the periosteal and endosteal ends.

Observations After Twenty-Two Days.—Blood cells could still be seen within the labyrinth. A wedge-shaped mass of bone filled the perforation with the largest mass on the periosteal aspect (fig. 8). Fragments of old bone, sur-

rounded by new bone, remained. The linear fractures were filled with bone (fig. 9). There was no evidence of osteoclastic absorption of fragments or callus.

Observations After Thirty Days.—The callus in the periosteal surface of the capsule appeared to have undergone reduction in size compared with less mature lesions, but osteoclastic activity was not seen. Osteogenesis was proceeding in

Fig. 10.—Photomicrograph (× 43.6) of a thirty day lesion at the site of perforation, showing it well filled with new bone in which can be seen some connective tissue (*F*) and a large blood vessel (*V*). The callus on the periosteal aspect of the capsule has been reduced in size. A group of large fragments of viable bone are seen displaced inward along with the attached spiral ligament. New bone, probably of endosteal origin, is present at *R*.

the depth of the fracture, in part probably by metaplasis of the connective tissue in the spiral ligament, as well as in delicate connective tissue arising from the

endosteum and adjacent spiral ligment (fig. 10). The connective tissue cells within the spiral ligament, under the influence of trauma and hemorrhage, laid down bone. This calcification of the spiral ligament extended for some distance from, but was continuous with, the site of fracture (fig. 11).

Observations After Thirty-Six Days.—In one area of the callus in the inner surface of the perforation, evidence of absorption of bone by mononuclear cells, was present. Few spicules of bone remained, some having been removed probably by "creeping replacement" by the adjacent new bone. Cartilage was not seen in any of the specimens examined.

Localized Periosteal Injuries.—The experiment of injuring the periosteum by scratching was carried out to determine the reaction of the periosteum of the

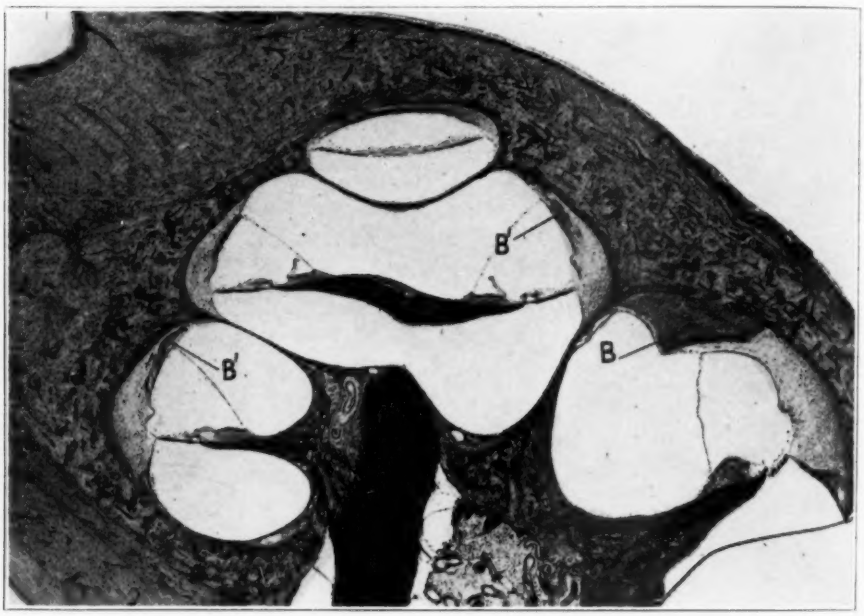

Fig. 11.—Photomicrograph (× 47.5), showing new bone adjacent to the site of the perforation in the basal coil (*B*) and calcification extending within the spiral ligament (*B'*) throughout the basal and part of the middle coil.

otic capsule to trauma. In brief, specimens about three weeks old all showed a thin layer of new bone opposed to the old bone of the capsule, together with a thickening of the periosteum. A row of osteoblastic cells in the deepest portion of the periosteum overlay the new bone. In general, healing of the perforation in the bulla proceeded at the same rate as that of the cochlear injury. However, in contrast to the limited activity in the inner or endosteal aspect of the injury to the labyrinth, the inner aspect of the wall of the bulla at the site of the perforation showed the principal activity. The bulla was lined by a loosely attached, delicate transparent membrane which responded actively to direct injury or partial stripping. A marked hyperplasia of the connective tissue in it took

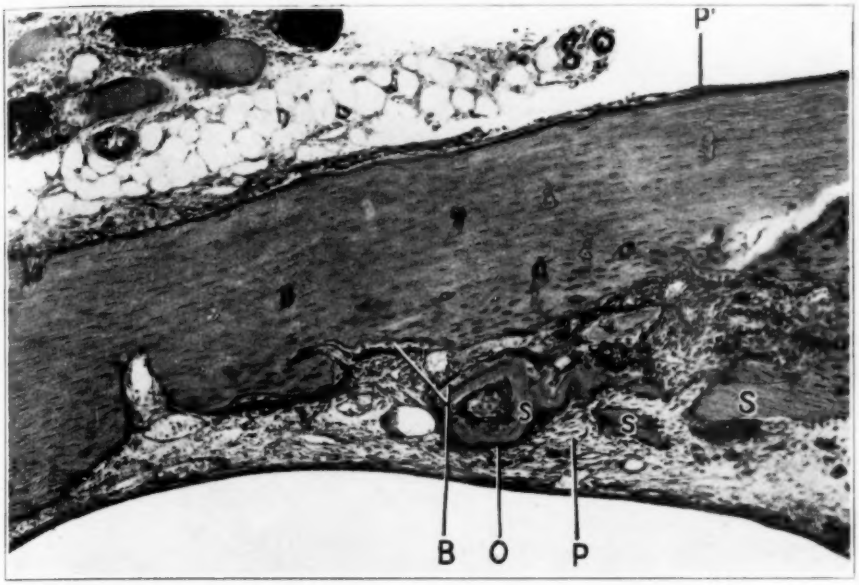

Fig. 12.—Photomicrograph (× 42.7), showing a three day old injury of the wall of the bulla adjacent to the site of perforation; note the marked activity of the periosteum (*P*) on the inner surface in contrast to the lack of reaction on the outer surface (*P'*). Spicules of bone (*S*) are surrounded by a layer of osteoblasts (*O*), and formation of new bone is beginning at *B*.

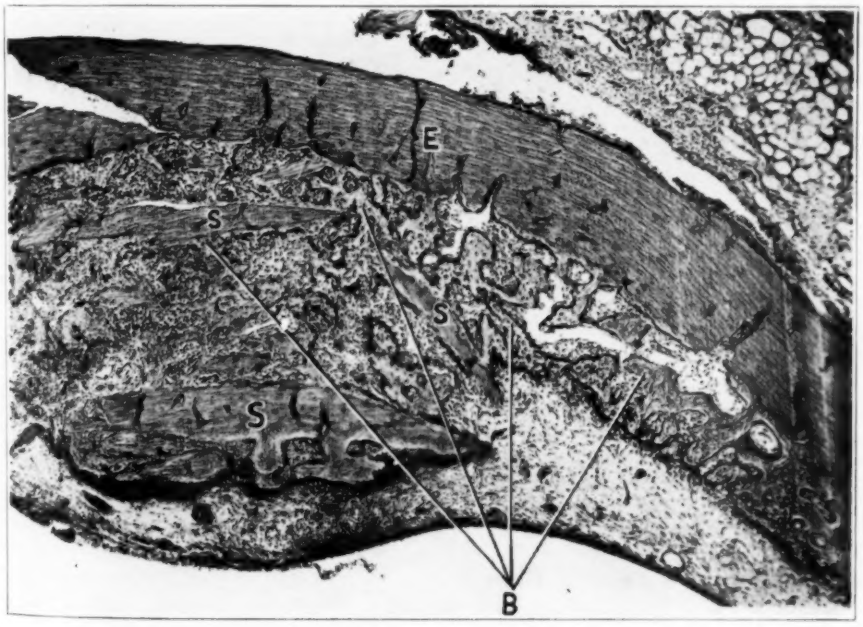

Fig. 13.—Photomicrograph (× 54.4) of a six day old lesion of the wall of the bulla adjacent to the opening made in it to approach the cochlea; note the marked osteogenic activity in the inner aspect of the wall of the bulla and the lack of it in the outer aspect; extensive new bone (*B*), surrounded by a layer of osteoblasts, is seen in the deeper layers of the periosteum adjacent to the old bone (*E*); new bone is being applied against the bone chips (*S*).

place, followed by an extensive osteogenesis (figs. 12 and 13). In the the twenty-two day specimen, the old bone of the bulla was seen to be invaded by vascular buds coming from the endosteal callus resulting in a firm interdigitation between callus and old bone (fig. 14). In general the border between callus and old bone was distinct. The reason for the small amount of activity on the outer aspect of the wall of the bulla probably lies in the fact that in the surgical exposure of the bulla the periosteum, including its cambium, was rubbed away over a large area before the perforation in the bulla was made.

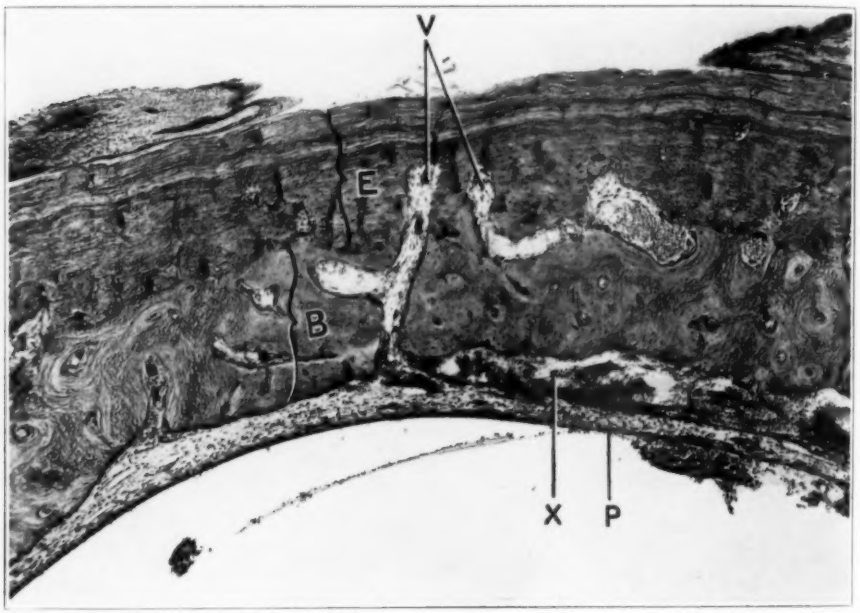

Fig. 14.—Photomicrograph (× 54.4), showing the appearance of the wall of the bulla twenty-two days after injury; note the thick layer of new bone (*B*) applied to the old bone (*E*), with vascular spaces (*V*) on the inner aspect eroding the old bone and permitting interdigitation between the two layers of bone. Stripping away of the mucoperiosteum (*P*) in one area with hemorrhage (*X*) occurred at the second operation when the animal was killed.

COMMENT

The principal factor in the process of healing of a complete fracture or perforation of the otic capsule as seen in these specimens is the activity of the periosteal layer. This layer of tissue is continuous with the submucosa. Its innermost aspect is composed of active osteogenic tissue, probably continuous with the haversian systems. The periosteum increases in thickness and grows into the fracture and perforation, replacing the blood clot and surrounding the spicules of bone chipped

from the capsule. At the same time, cells in the deeper layer of the fibrous periosteum differentiate as a layer of osteoblastic cells, the cambium, and become directly opposed to the spicules or fractured surfaces. This new bone has a definite architecture, arranged around an individual blood supply and with cells parallel to the line of fracture or at right angles to the cells in the bone of the capsule, so that in the line of fracture no difficulty exists in differentiating callus from the adjacent bone of the capsule. Evidence of the connective tissue and blood vessels entering the linear fracture and perforation from the periosteal aspect can be seen even after thirty-six days, when formation of bone is far advanced. The periosteum for a considerable distance from the site of perforation is injured by the operation and responds by formation of callus, just as in the experiments in which it alone was injured, by scratching. Excessive callus, particularly in the periosteal aspect but also on the endosteal aspect of the perforation, gradually becomes absorbed to conform more closely to the adjacent bony contours, preserving the labyrinthine spaces but without osteoclastic activity. Often the perforating needle tends to push ahead of it the soft tissue lying adjacent to the inner wall of the labyrinth. This space, formed by the stripping away of the soft tissue, such as spiral ligament, from the capsule, fills with blood and spicules of bone, and into it grows osteogenic tissue from the periosteum. The endosteum of the otic capsule shows little reaction in the process of repair in contrast to its activity in the repair of long bones.[7] The bony laminas separating the coils of the cochlea show little osteogenic activity in response to injury, but the cells covering them throw out a meshwork of delicate connective tissue, in which new bone may later be laid down. The bone of the capsule forming the wall of the fracture and perforation in the endochondral layer does not enter into the ossification. The connective tissue cells in the spiral ligament at the site of the perforation and for some distance beyond may take on osteogenic properties and lay down considerable new bone, as a result of direct trauma and hemorrhage.

Blood within the labyrinth, arising as a result of trauma, appears to have little effect on the process of healing. Its presence or absence in the various specimens did not appear to influence the degree of repair. Its presence in some specimens from animals which had lived thirty days after a minute perforation was made in the cochlea speaks against a rapid disappearance either by absorption or as a result of circulation of labyrinthine fluids to the subarachnoid space. The fate of blood cells is not clear. Pigment or cellular débris is sometimes seen, but there is little histologic evidence indicating, as some have suggested, that it

7. Bast, T. H.; Sullivan, E. D., and Geist, F. D.: Anat. Rec. **31**:225 (Nov.) 1925.

acts as an irritant. The organ of Corti, distant from the site of perforation, is histologically normal.

In the specimens from animals with otitis media, invasion of the labyrinth via the site of the injury was always seen and resembled the pathologic process which is seen in the human being with a fractured labyrinth in whom labyrinthitis develops following otitis media. In the experimental animals the possibility that the infection in the middle ear immediately followed the operation cannot be excluded. However, the specimens show that the blood supply extends inward from the periosteal surface of the callus as far as the endostium, possibly even anastomosing with the blood supply to the labyrinth. The persistence of these vascular spaces through the lines of fracture provides an easy pathway for extension of infection from subsequent otitis media to the labyrinthine spaces.

The endochondral and endosteal layers of the capsule of the labyrinth, in the rabbit and dog as in the human being, because of its architecture and early mature development, show little histologic evidence of activity in response to metabolic or mechanical stimulus after birth. It is not undergoing constant change, as does skeletal bone, for example. The new bone laid down in a linear fracture of the labyrinth will thus remain distinct from, and will not be invaded or replaced by, the adjacent bone of the capsule. The irregularities of the wall of a linear fracture, resulting from exposed lacunas of haversian canals and osseous cells, permit dovetailing of the callus with the adjacent capsule because of the invasion of these lacunas by osteogenic tissue and subsequent ossification, and thus a more firm union results between callus and otic capsule. The resultant callus may be described as a tightly fitting bony plug, filling the perforation in the capsule, produced principally by the periosteum and usually flaring on the outer and inner aspects. However, the blood vessels that grow in with the new bone, uniting the blood vessels in the submucosa of the middle ear with the intralabyrinthine vessels, persist and afford a direct permanent communication between the middle ear and the labyrinth.

The contention of some that delayed union in the case of fracture in a human being may be due to the invagination of mucous membrane on the promontory into the fracture is not borne out by the observations on these specimens. It appears likely that the principal reason for the small degree of osteogenesis in many of the fractures in the human specimens is the shattering effect on the capsule of injuries to the head resulting in the relatively small trauma to the periosteal layer. In the fractures involving the endosteal or the endosteal and the endochondral layer only, fibrous union occurs because of the evidently poor osteogenic properties of these layers of the capsule in cases of aseptic injury.

SUMMARY

A small perforating injury of the capsule of the labyrinth is sealed by a blood clot after a few hours. Swelling of the adjacent periosteal layer is observed after the first day. The fibrous tissue proliferating from the periosteum then invades the blood clot and replaces it in three days. At the same time a differentiation of the periosteum into osteogenic layer, or cambium, and fibrous layer occurs. By the fifth day apposition of new bone begins against bone chips and the surfaces of the fracture as well as on cortex where the periosteum was injured. By the end of the second week most linear fractures are well filled with bone, along with vascular tissue, which has grown in with it from the periosteum. These blood vessels continue into the depth of the perforation, probably anastomosing with the intralabyrinthine vessels. The new bone and its nutrient vessels remain distinct from the adjacent bone of the capsule. At the end of four weeks excess periosteal callus and to a lesser degree endosteal callus are removed, and the activity of the tissues at the site of injury appears to have reached equilibrium. New bone gradually invades and replaces them without definite evidence of osteoclastic absorption in it or in the periosteal callus. Few fragments or spicules are to be seen in the callus after thirty days. The endochondral and the endosteal layer of the capsule forming the walls of the perforation show no evidence of osteogenic activity. The connective tissue of the endosteum and the connective tissue covering the lamina between the coils and in the spiral ligament respond to injury by laying down a meshwork of delicate fibrous tissue, in part of which ossification may begin by the eighth day. Some of the spiral ligament itself at the site of the injury and for some distance away ossifies. Small localized perforating aseptic injuries to the cochlea of the rabbit do not result in a progressive obliterative process within the labyrinth, such as is produced by a suppurative process within the labyrinthine spaces.

ACUTE MASTOIDITIS FROM THE SURGICAL POINT OF VIEW

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NEW YORK

The purpose of this report is to present a review of a series of cases of acute and recurrent mastoiditis out of the experience and from the point of view of the surgeon. While no new or startling information will be presented, certain facts concerning the disease will stand out as being of fundamental importance. It is to be noted that these cases represent the experience of a single surgeon. This point is to be emphasized, because the variable personal factors which influence other reports from entire hospital staffs are minimized in a study of this nature.

The cases which I review here are those of a series of patients with acute and acute recurrent mastoiditis operated on at the Bronx Hospital during the years 1932 to 1938. There was a total of 275 cases of acute mastoiditis and 43 cases of acute recurrent mastoiditis, or 318 cases in all.

In the series of cases of acute mastoiditis the distribution between the sexes was approximately equal, there being 128 males and 147 females, or 46.5 per cent and 53.5 per cent, respectively. In the series of cases of acute recurrent mastoiditis the males predominated, there being 25 males and 18 females, or 58.2 per cent and 41.8 per cent, respectively. It is of interest to note the relative frequency of mastoiditis on the two sides. This is shown in table 1.

Like acute otitis media, which it so frequently complicates, mastoiditis is a disease of childhood. In the series of cases of acute mastoiditis 44.7 per cent of the patients were 5 years old or less, and 79.3 per cent were 10 years old or less. Acute recurrent mastoiditis also was seen most frequently in children. The distribution according to age is seen in table 2.

In discussing age groups with reference to mastoiditis, it is of interest to study how long after primary mastoidectomy acute recurrent mastoiditis occurred. These data are shown in table 3. In many cases primary mastoidectomy was performed elsewhere and by another surgeon, and the information contained in table 3 was obtained from 39 of the 43 patients.

Study of table 3 will show that in nearly 70 per cent of the cases acute recurrent mastoiditis occurred within three years of the primary mastoidectomy and in one fourth of the cases it occurred during the first year after the primary mastoidectomy.

Practically all attacks of mastoiditis are preceded by infection of the middle ear. Whether drainage had been established by paracentesis or by spontaneous rupture, in most of the cases there was discharge from the meatus. Tables 4 and 5 have therefore been prepared in an attempt to correlate the duration of the discharge in these cases of

TABLE 1.—*Frequency of Mastoiditis on the Two Sides*

	Right	Percentage	Left	Percentage	Bilateral	Percentage
Acute mastoiditis	134	49.0	113	41.0	28	10.0
Acute recurrent mastoiditis	20	46.6	22	51.1	1	2.3

TABLE 2.—*Distribution of Mastoiditis According to Age*

Age (Years)	Acute Mastoiditis (275 Cases)			Acute Recurrent Mastoiditis (43 Cases)	
	No. of Cases	Percentage		No. of Cases	Percentage
0 to 1	36	13.1		0	0.0
1 to 2	33	12.0		3	7.0
2 to 3	14	5.1	44.7%	1	2.3
3 to 4	21	7.6		4	9.3
4 to 5	19	6.9		7	16.3
5 to 6	39	14.2	79.3%	6	14.0
6 to 7	22	8.0		3	7.0
7 to 8	16	5.8		7	16.3
8 to 9	11	4.0		2	4.6
9 to 10	7	2.5		1	2.3
10 to 15	19	7.0		6	14.0
15 to 20	5	1.8		2	4.6
20 to 30	15	5.5		1	2.3
30 to 40	12	4.4		0	0.0
40 to 50	5	1.8		0	0.0
50 or over	1	0.4			

TABLE 3.—*Number of Years Since Previous Mastoidectomy in Cases of Acute Recurrent Mastoiditis*

Years	No. of Cases	Percentage
0 to 1	10	25.6
1 to 2	11	28.3
2 to 3	6	15.4
3 to 4	3	7.7
4 to 5	3	7.7
5 to 6	3	7.7
6 to 15	3	7.7

acute mastoiditis with the onset and duration of the mastoid involvement. Table 4 is based on the histories of 257 cases in which the duration of the discharge was stated. Table 5 is somewhat less accurate, and the data were ascertained from the date at which mastoid involvement was established by physical and roentgen examination and study of the symptoms in 244 cases. The same data have been tabulated for the cases of acute recurrent mastoiditis.

Analysis of the tables just discussed shows that discharge from the meatus had been present for fifteen days or less in 59.7 per cent of the cases of acute mastoiditis when mastoid involvement became apparent and in only 14.4 per cent of cases in which mastoiditis appeared had the discharge been present for five days or less. However, in the cases of acute recurrent mastoiditis 40 per cent of the patients had had discharging ears for five days or less, and in 85.7 per cent of the cases the discharge had been present for fifteen days or less. In other words, acute mastoiditis occurs much earlier after infection of the middle ear

TABLE 4.—*Duration of Discharge*

	Acute Mastoiditis (257 Cases)		Acute Recurrent Mastoiditis (35 Cases Only)	
Duration (Days)	No. of Cases	Percentage	No. of Cases	Percentage
None	6	2.3	3	8.5
1 to 5	37	14.4	14	40.0
6 to 10	63	24.6	9	25.7
11 to 15	53	20.7	7	20.0
16 to 20	7	2.7	1	2.9
21 to 30	69	26.8	0	0.0
31 to 40	7	2.7	1	2.9
41 to 50	8	3.1	..	....
51 and over	7	2.7	..	....

TABLE 5.—*Duration of Symptoms Indicating Mastoid Involvement*

	Acute Mastoiditis (244 Cases)		Acute Recurrent Mastoiditis (41 Cases)	
Duration (Days)	No. of Cases	Percentage	No. of Cases	Percentage
1	15	6.1	0	0.0
2	61	25.0	9	21.9
3	47	19.3	11	26.9
4	17	7.0	2	4.8
5	17	7.0	1	2.4
6 to 10	50	20.5	15	36.8
11 to 15	21	8.6	2	4.8
16 to 20	3	1.2	1	2.4
21 to 25	10	4.1		
26 to 30	3	1.2		

in cases in which mastoiditis has previously been present. Table 5 shows that with either infection about half of the patients are admitted when the mastoiditis has been present three days or less.

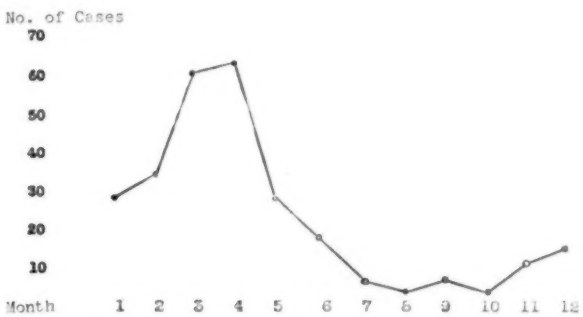
Acute mastoid disease shows a marked seasonal variation of frequency. It is most frequent during the months of midwinter and spring. This fact is clearly shown in table 6 and in the chart.

I shall not discuss the symptoms of mastoiditis in detail here, because to do so would carry me beyond the scope of this paper; nevertheless, the frequency of the more important symptoms and signs deserves consideration. Subjective pain over and about the mastoid process was present in 266 of the cases of acute mastoiditis, or 96.7 per cent. Pain was present in 100 per cent of the 43 cases of acute

recurrent mastoiditis. Tenderness over the mastoid process was present in 264 of the cases of acute mastoiditis, or 96 per cent. Tenderness was present in 100 per cent of the 43 cases of acute recurrent mastoiditis.

TABLE 6.—*Seasonal Variation in the Incidence of Mastoiditis*

Month	Acute Mastoiditis (275 Cases)		Acute Recurrent Mastoiditis (43 Cases)	
	No. of Cases	Percentage	No. of Cases	Percentage
January	29	10.5	6	14.0
February	36	13.1	5	11.6
March	61	22.0	6	14.0
April	63	23.0	9	21.0
May	28	10.2	3	7.0
June	18	6.6	3	7.0
July	6	2.2	3	7.0
August	3	1.1	1	2.3
September	6	2.2	0	0.0
October	1	0.3	4	9.1
November	10	3.7	0	0.0
December	14	5.1	3	7.0



Seasonal variation in the incidence of acute mastoiditis (based on 275 cases).

Swelling or edema of the mastoid process or in the periotic region was present in 85 cases of acute mastoiditis, or 30.9 per cent. Swelling was present in 26 of 43 cases of acute recurrent mastoiditis, or 64.6 per cent, which is more than double the frequency in the cases of acute mastoiditis. Roentgen reports in every case of acute mastoiditis indicated clouding of the mastoid cells, cellular destruction and exudate. In the cases of acute recurrent mastoiditis, in which mastoiditis was obviously present, an insufficient number of roentgenograms were taken to justify drawing any conclusions worth discussing.

The variation in temperature in cases of mastoiditis is brought out in table 7. It will be noted that the great majority of patients had fever, with the temperature ranging between 100 and 102 F.

Study of the blood in the cases of acute mastoiditis showed that there is nearly always polymorphonuclear leukocytosis. Since the incidence of mastoiditis in childhood is high and since relative lymphocytosis is normal in children, differential blood counts in cases of mastoiditis are

somewhat confusing, except that as a rule there is a "shift to the left," or an increase in immature polymorphonuclear leukocytes. The variations in total number of leukocytes are shown in table 8.

All of the patients with mastoiditis were operated on under general anesthesia. The younger patients had open mask ether anesthesia, while the older children and adults had gas, oxygen and ether. Of the patients with acute mastoiditis 227 had ether only, and 48 had nitrogen monoxide, oxygen and ether. Of the patients with acute recurrent mastoiditis, 36 had ether only, and 7 had nitrogen monoxide, oxygen and ether. For children ethyl chloride was frequently employed to induce anesthesia before administration of ether was begun.

TABLE 7.—*Variation in Temperature of Patients with Mastoiditis*

	Acute Mastoiditis (275 Cases)		Acute Recurrent Mastoiditis (41 Cases Only)	
Temperature (F.)	No. of Cases	Percentage	No. of Cases	Percentage
99 to 100	42	15.2	6	14.6
100 to 101	78	28.4	12	29.2
101 to 102	89	32.4	13	31.7
102 to 103	36	13.1	7	17.0
103 to 104	25	9.1	2	5.0
104 to 105	5	1.8	1	2.5

TABLE 8.—*Variations in Total Leukocyte Count in Cases of Mastoiditis*

	Acute Mastoiditis (225 Cases)		Acute Recurrent Mastoiditis (33 Cases)	
Total Leukocytes	No. of Cases	Percentage	No. of Cases	Percentage
5,000 to 10,000	15	6.6	1	3.0
10,000 to 12,000	35	15.6	3	9.0
12,000 to 15,000	60	26.6	3	9.0
15,000 to 20,000	70	31.0	17	52.0
20,000 to 25,000	33	14.7	7	21.0
25,000 and over	12	5.5	2	6.0

Among the 275 cases of acute mastoiditis there were 226 cases in which simple mastoidectomy was performed. In the remaining 49 cases other operative procedures were employed in addition to simple mastoidectomy. In 23 of the latter cases the sinus plate was so involved that it had to be removed partially or wholly, so that more or less of the lateral sinus was exposed, without damage to the sinus itself except in 5 cases of sinus thrombosis in which the lateral sinuses were explored. In 14 cases the dura had to be exposed on account of involvement of overlying bone. In the remaining 12 cases both sinus and dura were exposed. Of the 43 cases of acute recurrent mastoiditis, simple secondary mastoidectomy was performed in 34; in this process any overlooked or regenerated cells which had again become involved in acute mastoid infection were exenterated, so that only clean and uninvolved bone remained. In 1 case radical mastoidectomy was performed.

In 3 cases the sinus and dura were exposed as previously described. In 1 case the dura alone was exposed, and in another the sinus alone was exposed. In the remaining 3 cases of acute recurrent mastoiditis, simple incision and drainage of subperiosteal abscesses sufficed. These procedures are listed in table 9.

Other operative procedures than those listed included ligation of the jugular vein in the neck after exploration and packing of the sinus in several cases of sinus thrombosis, incision and drainage of cervical abscesses at the time of mastoidectomy and removal of the tip of the mastoid process in 2 cases of von Bezold's abscess.

TABLE 9—*Operative Procedures in 318 Cases of Mastoiditis*

Operation	Acute Mastoiditis		Acute Recurrent Mastoiditis	
	No. of Cases	Percentage	No. of Cases	Percentage
Simple mastoidectomy	226	82.2	..	....
Simple secondary mastoidectomy	..	....	34	79.1
Radical mastoidectomy	..	....	1	2.3
Exposure of sinus	23	8.4	1	2.3
Exposure of dura	14	5.1	1	2.3
Exposure of sinus and dura	12	4.3	3	7.0
Incision and drainage	..	....	3	7.0

TABLE 10.—*Bacteria Found in Culture of Mastoid Pus* *

Organism	Acute Mastoiditis (242 Cases)			Acute Recurrent Mastoiditis (23 Cases)		
	No. of Cases	Percentage		No. of Cases	Percentage	
Hemolytic streptococcus	103	42.6	88.5%	11	48.1	87.1%
Nonhemolytic streptococcus	62	25.7		6	26.0	
Streptococcus viridans	49	20.2		3	13.0	
Pneumococcus	7	2.9		..	....	
Staphylococcus albus	3	1.2		..	....	
Staphylococcus aureus	1	0.4		..	....	
Bacillus subtilis (contaminant)	2	0.8		..	....	
Proteus vulgaris (contaminant)	1	0.4		..	....	
Haemophilus influenzae	..	....		1	4.3	
Sterile culture	14	5.8		2	8.6	

* The classification of hemolytic and nonhemolytic streptococci was not based on strict cultural criteria; the presence or absence of hemolysis was determined by the use of plates made with human blood.

Culture of the pus found in the mastoid at operation revealed that streptococci are by far the most frequent organisms concerned in cases of mastoiditis. Pneumococci also, especially in adults after respiratory infection, were found in several cases, as were staphylococci and a few others (table 10).

Blood culture was not done as a routine in these cases, except when high temperature, chills or complications indicated their need. In the cases of acute mastoiditis, of 21 reported blood cultures, 18 were sterile and 3 showed streptococci. In 2 of the 3 cases of streptococcic infection

thrombosis of the lateral sinus was found. All 3 patients recovered. Blood cultures were sterile in all cases of acute recurrent mastoiditis in which they were made.

The complications which occurred both before and after operation in these cases of mastoiditis are listed in tabular form for the sake of

TABLE 11.—*Complications of Acute Mastoiditis* and Their Outcome*

Complication	No. of Cases	Outcome
Sinus thrombosis	5	4 patients recovered; 1 died
Streptococcic meningitis†	2	Both patients died
Petrositis	2	1 patient recovered; 1 died
Von Bezold's abscess	2	Both patients recovered
Varicella	4	All patients recovered
Erysipelas	4	All patients recovered
Acute hemorrhagic nephritis	6	All patients apparently recovered
Bronchopneumonia	2	Both patients recovered
Lobar pneumonia	1	Patient recovered
Cervical abscess	3	All patients recovered
Acute pyelitis	2	Both patients recovered
Palsy of the facial nerve (preoperative)	2	Both patients recovered after operation

* In the series of cases of acute recurrent mastoiditis the only complications were erysipelas in 2 cases, in both of which the patient recovered, and bleeding from the edges of the skin in 1 case, in which the condition was easily controlled.

† These cases came under observation before sulfanilamide, which might have influenced the course of the disease, was introduced.

TABLE 12.—*Duration of Postoperative Hospitalization*

Days	Acute Mastoiditis (271 Cases, Omitting the 4 of Fatal Termination)		Acute Recurrent Mastoiditis (43 Cases)	
	No. of Cases	Percentage	No. of Cases	Percentage
3	..	....	2	4.8
4	..	....	1	2.4
5	2	0.7	2	4.8
6	11	4.0	6	13.8
7	85	31.5	13	30.0
8	59	21.7	9	20.7
9	27	10.0	2	4.8
10	21	7.7	1	2.4
11	16	6.0	3	6.9
12	15	5.5	1	2.4
13 to 15	7	2.5	1	2.4
16 to 20	14	5.2	..	....
21 to 30	14	5.2	2	4.6

simplicity, together with the outcome. The seriousness of several of these complications, such as sinus thrombosis and meningitis, is too well known to warrant further comment, except for reemphasis. There were 5 patients with sinus thrombosis in this series, 4 of whom recovered. There were 2 patients with streptococcic meningitis, both of whom died (table 11).

In the entire group of 318 cases of acute mastoiditis there were 4 of fatal termination, a mortality of 1.2 per cent. These 4 included 2 of streptococcic meningitis,[1] 1 of sinus thrombosis and 1 of petrositis.

One last point which is of interest in cases of acute mastoiditis is the duration of hospitalization after operation. The great majority of the patients whose condition was uncomplicated remained from seven to nine days; in cases in which complications arose a longer postoperative stay in the hospital was required (table 12).

SUMMARY

I have presented a series of 275 cases of acute mastoiditis and 43 cases of acute recurrent mastoiditis in which I operated at the Bronx Hospital during the years 1932 to 1938. I have shown in tabular form the frequency according to sex, age and side involved, the more important symptoms and signs and the seasonal variations and have tabulated the operative procedures, the bacteria found by culture at operation and the complications. The mortality was found to be 1.2 per cent.

2021 Grand Concourse.

1. In these cases death occurred before the introduction of sulfanilamide, which might have influenced the outcome.

AIR-BORNE DROPLET INFECTION

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Although I make no claim to personal proficiency in the special field of bacteriology, the hazard of air-borne infection encountered in the clinical practice of otolaryngology has piqued my curiosity to a considerable extent.

The theory of air-borne contagion had its illustrious origin in remotest antiquity, for some four hundred years before Christ it was written by Hippocrates that "according to all appearances, the cause of disease should be found in the air." In 1861, Louis Pasteur animated this ancient concept by proving that air is peopled with invisible germs, which somehow bring about fermentation and putrefaction. Thus were born both a science and a theory—the science of bacteriology and the germ theory of disease.

Pasteur's discovery was like a new religion, for it was not long before its apostles were devoutly at work. Of all the proponents of this new and inclusive theory surely none were more vocal or more demonstrative than Joseph Lister and John Tyndall in England. Soon a haze of carbolic acid spray hung over Lister's surgical amphitheater, and every surgeon was schooled in antisepsis and the use of antiseptics. The pendulum was swinging, and for the next twenty years swung far beyond center, for the belief became all but universal that air was the vehicle of contagion.

Time passed, and knowledge of bacteriology increased, especially during the last two decades of the nineteenth century. By then the specific agents of many diseases were identified in rapid succession and their transmission by routes other than air disclosed. But what was even worse for the prestige of the theory of transmission of infection by air-borne agents was the failure to demonstrate in air the presence of recognized pathogenic bacteria.

In 1898, Flügge discredited the theory of air-borne infection still more when he failed to recover nasopharyngeal organisms on plates exposed farther than a few feet from persons coughing and sneezing and so concluded that organisms settled out in short distances and brief intervals.

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In 1914, Chapin [1] reviewed seriatim most of the commonly known diseases and showed that their dissemination by air is either untenable or unlikely, emphasizing the low incidence of cross infection in hospitals for contagious diseases. Chapin's contribution seemed opposed to the concept of Hippocrates and the conclusion of Pasteur that air is the vehicle of contagion, and it apparently sounded the death knell of this theory.

This condition existed until about 1936, when publications by Wells and Wells [2] and Chope and Smillie [3] reopened the whole problem. Working in the Department of Public Health Administration and Sanitary Engineering at Harvard University, Wells and Wells have developed a special instrument for the study of controlled atmospheres, and by atomizing cultures of bacteria into these atmospheres they provided a means of noting the dispersion of bacteria in air and the effect of physical and chemical agents on their viability. Contrary to the results of Flügge's experiments, it was found that droplets expelled from the nose and throat by sneezing, coughing and the like do not necessarily and immediately fall to the ground within a short distance from their source but may be transported for distances varying with their size, composition and rate of evaporation.

It is estimated that the residues after evaporation of droplets of body fluids less than 0.1 mm. in diameter are so small that their behavior in air resembles that of smoke rather than that of the droplets described by Flügge. Wells and Wells demonstrated this phenomenon by atomizing various liquids into the dark interior of the Harvard experimental tank, through which a strong beam of light was projected. They found that distilled water evaporates and leaves no residue in the beam but that a liquid containing a substance in solution (such as sodium chloride) after evaporation in the chamber leaves a nuclear residue resembling fog, which is clearly revealed by the Tyndall effect. Liquid suspensions of micro-organisms were similarly atomized into the tank, and the presence of the organisms for hours and days was quantitatively demonstrated by the air centrifuge.

It was therefore concluded that infection transmitted through the air takes one of two forms, according to the size of the infected droplet. The more obvious form, and the one recognized by Flügge, may be termed droplet infection proper, as it is produced by droplets larger than 0.1 mm., which settle within a short radius of their source before they

1. Chapin, C. V.: The Air as a Vehicle of Infection, J. A. M. A. **62**:423 (Feb. 7) 1914.

2. Wells, W. F., and Wells, M. W.: Air Borne Infection, J. A. M. A. **107**: 1698 (Nov. 21) 1936.

3. Chope, H. D., and Smillie, W. G.: Air Borne Infection, J. Indust. Hyg. & Toxicol. **18**:780 (Dec.) 1936.

can dry. However, after the droplet has settled and evaporated, the infectious material may be lifted as dust, thus producing air-borne infection, which is the second form of transmission of disease by air. This second type is produced by the dried residues of infected droplets less than 0.1 mm. in diameter, which remain suspended in air for longer intervals and are transported greater distances. Thus it is seen that droplet infection is essentially localized and concentrated, while infection broadcast by nuclei or residues of droplets is more dispersed and dilute. Likewise it was demonstrated that micro-organisms can remain suspended alive in air for periods which may permit their wide dissemination in a viable state.

The Harvard workers also recognized the fundamental importance of ascertaining the relative viability of various types of organisms pathogenic for man. They found that the bacteria which infect the respiratory tract, when carried in droplet nuclei, are more viable than are those that infect the intestines, the former being found alive as long as several days after dissemination in the experimental tank. The group of bacteria that infect the respiratory tract included Pneumococcus type I and Bacillus diphtheriae.

As a result of these and other experiments, Wells and Wells graphically concluded that "under conditions of crowding in enclosed rooms we are breathing one another's nasopharyngeal flora as we once drank each other's intestinal flora in our water supplies and the consequences of such practices become a study in sanitary science." In explanation of the lack of cross infection in hospitals, emphasized by Chapin as evidence controverting the theory of the spread of contagion by air-borne agents, these authors pointed out that in the interpretation of this evidence the factors of immunity, of subclinical infections and of preclinical infectiousness have been overlooked.

In answer to those practical people who ask what can be done about it, granted that air can be contaminated by pathogenic organisms, it may be pointed out that ultraviolet radiation has been found highly efficient as a bactericidal agent for contaminated air, especially in low humidity. An apparatus is currently on the market for this very purpose.

My particular interest in air-borne infection was stimulated by my experiences in using a nasal oil atomizer of superior grade and well known make. I bought this atomizer with the explicit understanding that it was the most efficient type available. Now my only complaint is that it is definitely too efficient—in fact, so efficient that if it atomizes at all, even with the minimum of pressure, it produces a spray almost like smoke, which when introduced into one nostril returns immediately through the other nostril and the mouth also, if open, and envelops the operator and floats off into the room a distance of several feet.

Generally the patients take unrestrained delight in adding to the display by inhaling during the atomization and then blowing out a cloud of smoke, often, I regret to add, directly into the operator's face.

After listening for some time to the complimentary remarks of my patients on the evident efficiency of this procedure, all the while receiving large second hand doses of the medicament, I began to wonder if I might not be inadvertently subjecting myself needlessly to air-borne droplet infection from the patient whom I was treating. To answer this question I began a series of tests with patients suffering from various ailments. A total of 72 cultures on blood agar were made from 24 patients, but not more than 1 patient was tested in any one day. The conditions for which these patients were being treated at the time of making the cultures included acute and chronic nasopharyngitis, acute and chronic sinusitis, acute and chronic catarrhal tubotympanitis, acute tracheitis and laryngitis, chronic suppurative otitis media, nasal allergy and polypi and laryngeal cancer.

The technic of making the cultures was as follows:

> The patient selected for examination was seated in a treatment chair, and a Petri dish containing blood agar was opened and placed on a shelf about 3 feet (91 cm.) from the patient but not in line with particles that might be ejected from his nose and throat. This culture medium was left exposed to the air of the room during the course of the patient's treatment, usually five to ten minutes. A second Petri dish was opened and the culture medium sprayed with the atomizer which next was used in spraying the patient's nasal passages. This Petri dish was immediately closed. The third test was made by atomizing through one nasal passage and catching the return flow from the other nostril in a third Petri dish which was opened and held by an assistant 6 inches (15 cm.) in front of the patient's face and in such a position that the contained culture medium was exposed to the full effect of the escaping vapor.

Early in the experiment, I had imagined that tests of patients with acute conditions in the respiratory tract would show the greatest amount of air-borne contagion, but this view proved erroneous, as the greatest evidence of air-borne infection occurred in cases of chronic nasopharyngitis, chronic suppurative otitis media and laryngeal cancer, in the order named. The explanation for this apparent discrepancy may lie in the flushing action on nasopharyngeal bacteria of the excessive secretions characterizing the acute inflammatory reaction and the consequent paucity of bacteria capable of being caught up in the nasal spray. Another factor tending to diminish the number of bacteria available for contamination of the air in cases of acute inflammatory reactions of the nose and throat is the lessening of the airway due to edema of the mucosa.

The organism that characterized all positive cultures was Staphylococcus albus, and only exceptionally were other organisms grown, i. e., Micrococcus catarrhalis and Staphylococcus aureus. These cultures were not studied after forty-eight hours, and only blood agar was used

as a culture medium; it is therefore possible that a more prolonged incubation and the use of additional mediums would have amplified the results. Wells and Wells have suggested that the recovery of the alpha streptococcus in the air and its quantitative estimation indicate the degree of nasopharyngeal contamination of that air, just as the quantitative estimation of Bacillus coli in water indicates the degree of intestinal contamination of the water. However this may be, it is a fact that the relative and overwhelming preponderance of colonies of Staph. albus in the culture of the nasopharyngeal spray in this experiment clearly demonstrates that this clinical procedure of nasal atomization is capable of instituting air-borne infection which constitutes a special hazard to the health not only of the otolaryngologist but also of the unsuspecting patient who breathes a previously contaminated atmosphere.

Although the great majority of cultures of all three types showed only from two to twelve colonies of Staph. albus after forty-eight hours of incubation, which suggests that the original infection was infinitely small and perhaps harmless, being frequently repeated in the course of a busy day of office routine such an infection could represent in the aggregate a bacterial dose of considerable magnitude. Chapin stressed the matter of bacterial doses in the causation of disease and pointed out the value of Winslow's work in this connection in the New York city schools.

Another and final thought in this consideration of air-borne infection has to do with a report by McCoy [4] of an outbreak of psittacosis among the personnel of the Hygienic Laboratory of the National Institute of Health in Washington. Eleven of the personnel became infected, and 1 died. Of this number, 8 had no connection with the investigation, and it was further established that person to person infection did not occur. In a discussion of this outbreak Chope and Smillie said:

> The epidemiological studies indicated strongly that the infection in this instance was air borne. If this disease, due to a filtrable virus, could be transmitted through the air as a medium, is it not possible that the virus of the common cold, the virus of influenza, of smallpox and measles, of encephalitis, and other conditions could be transmitted also through the same medium?

In conclusion, it is readily admitted that the early enthusiasm of Lister, Tyndall and many others for the belief that all disease was transmitted through the air was misguided, for epidemiologic evidence has shown that many diseases are transmitted through vehicles other than air. Yet on the basis of the evidence cited it would be a grave mistake to conclude without further proof that air plays no part in the transmission of communicable diseases.

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4. McCoy, G. W.: Psittacosis Among the Personnel of the Hygienic Laboratory, J. Infect. Dis. **55**:156 (Sept.-Oct.) 1934.

BUCCOANTRAL FISTULA: A METHOD OF CLOSURE

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The question of plastic closure of buccoantral fistulas has created little discussion in this country, and the literature accumulated on the subject is scanty. Many European authors have advocated various plastic procedures, most of which have passed into the discard. A plan of procedure is herewith described which has met with considerable success.

In 1651 Nathaniel Highmore [1] described a case of buccoantral fistula thus:

> The lower surface of this cavity (Antrum Genae) is very thin and frequently, upon drawing a tooth, is taken along with it, whereby the cavity is opened into the mouth. A gentlewoman who had the Dens Caninus drawn on account of an inveterate defluction of sharp humours, on thrusting a silver bodkin into the alveolus, was exceedingly frighted to find it pass, as it did, almost to her eyes. Upon further trial with a small feather stript of its plume, she was so terrifyd as to consult a Doctor and others, imagining nothing less than it had gone to her brain. But they considering the circumstances found that the feather had doubled only in this cavity.

As is well known, the roots of the upper posterior teeth are often in close relation with the maxillary sinus. However, a thin plate of bone usually supervenes between the root and the membranous floor of the sinus. As Lyons [2] has pointed out, one rarely sees the apical ends of the roots of the teeth lying freely exposed within the sinus. Nevertheless, infection about the upper teeth frequently erodes through the floor of the sinus and affects the sinus. The extraction of such a tooth establishes the fistulous tract. A fistula of this type tends to persist, usually demanding intranasal drainage of the sinus before the fistula can be closed. There are many other causes of buccoantral fistula, however. In many instances such a fistula owes its origin to the extraction of a vital tooth. In such cases the apical end is often fractured during the extraction, and too frequently the operator plunges in after the end of the root with an elevator, forcing it through the thin partition into the

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From the Western Pennsylvania Hospital.

1. Highmore, N., cited by Guthrie, D.: The Operative Closure of Oro-Maxillary Fistula, J. Laryng. & Otol. **47**:459-463, 1932.

2. Lyons, H.: The Treatment of Alveolar Fistula Secondary to the Extraction of Teeth, Tr. Am. Laryng., Rhin. & Otol. Soc. 1925, pp. 81-88.

antrum. It is better to remove such a root tip through a small window made in the buccal or lingual plate of the tooth socket, thereby avoiding the pressure in the direction of the long axis of the root which so often results in this mishap. In case the root is forced into the sinus, one should remove it immediately, preferably through a window made in the canine fossa, thereby avoiding enlargement of the alveolar fistula, which is usually the most dependent part of the sinus.

A third cause of buccoantral fistula is the destruction of bone incident to the presence of a tumor of the alveolus or of the maxillary sinus. Carcinoma or sarcoma of either site is an occasional instigator of this condition, and even an infected cystic tumor of the maxilla may result in a similar complication. A fourth group of conditions responsible for the formation of fistulas may be considered under the heading of inflammatory processes of the maxilla, including pyogenic osteomyelitis, syphilitic lesions of the maxilla and, more rarely, tuberculous and mycotic infections of bone. Destruction of bone incident to poisoning by the heavy metals may result in the formation of a fistula. In my series I have had 2 such fistulas following mercury poisoning (in press), and a similar one following "radium poisoning" (mesothorium). Other causative factors include trauma unassociated with the extraction of a tooth and persistence of fistulas after surgical intervention in a sinus.

It is noteworthy that after the establishment of a buccoantral fistula the patient often, if not usually, receives a form of treatment which is as disastrous as it is popular. Reference is made to the various types of sinal therapy instituted through the fistulous tract, including irrigations with or without the use of an indwelling tube, packing with gauze repeated over two or three day intervals and other equally disconcerting forms of therapy. Too, this therapy is often carried out regardless of the status of the sinus itself. Such packings are often performed in cases in which the sinus was accidentally opened during the extraction of a tooth and would probably close spontaneously if no treatment were directed to the complication. Many persistent buccoantral fistulas owe their presence to inexcusable packings through the alveolus.

It is often difficult to decide in a given case the best plan of procedure, since many fistulas of short duration will close spontaneously. If the patients could be seen immediately after the fistula had been established the tract should be closed by suture. However, usually several days has elapsed since the extraction of the tooth. In this circumstance two plans of procedure are open. First, the flaps about the fistulous tract are permitted to fall together; they are not sutured, and no alveolar therapy is instituted. In many such cases closure will occur spontaneously within a few days. However, if the fistulous tract is large

and the sinus is not acutely infected, a large nasal window is made, and the opening is closed by the operation to be described subsequently. In the clinic of the Western Pennsylvania Hospital no attempt is made to close a fistula in the presence of an acutely infected sinus. In this case the process is permitted to subside before an intranasal or plastic procedure is attempted. It is furthermore considered inexpedient to perform plastic closure of a fistula if the communication between the sinus and the mouth has been present for several days unless provision is also made for adequate nasal drainage, since in many such cases undoing of the plastic operation will later be required because of acute infection of the sinus. Strong [3] and Lyons [4] recommended the use of a denture over the fistulous opening to prevent particles of food from entering the sinus. Ordinarily my associates and I do not resort to this appliance and strongly object to the use of such a denture if any of the material of the denture projects into the orifice of the fistulous tract, since this will discourage spontaneous closure of the tract and will favor epithelization. As a permanent treatment for buccoantral fistula a denture or obturator is a poor substitute for a properly performed plastic operation.

Most fistulas have been present for weeks or months when they are first seen by the rhinologist or plastic surgeon. Although a variety of procedures have been recommended for closure of the fistulas, most authorities agree that the primary prerequisite for successful plastic repair is the establishment of adequate intranasal drainage. This may be accomplished by the method of preference of the operator. In our clinic we employ a modification of the Denker operation but agree with Hempstead [5] that if the sinus is markedly polypoid a more radical type of operation is indicated, such as the Caldwell-Luc.

Drury [6] advocated a nonplastic method for closure of the tract, employing liquor epispasticus B. P. (cantharidin 0.4 per cent w/v, with castor oil and colophony, in acetone), and Weih [7] advocated that after the infection in the sinus is cleared up, formation of scar tissue should be stimulated about the fistulous tract to effect closure.

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3. Strong, C. N.: Some Considerations of the Pathology and Treatment of Dental Infections of the Antrum, Proc. Roy. Soc. Med. **29**:1547-1552, 1936.

4. Lyons, H. R.: Empyema of the Antrum of Highmore Secondary to Extraction of Teeth, J. A. M. A. **78**:486-487 (Feb. 18) 1922.

5. Hempstead, B. E.: Intranasal Surgical Treatment of Chronic Maxillary Sinusitis, Arch. Otolaryng. **6**:426-433 (Nov.) 1927.

6. Drury, D. W.: A Procedure for the Cure of Antral Fistulae, Boston M. & S. J. **191**:1123-1124, 1924.

7. Weih, E. P.: Closure of Alveolar Fistula by Scar Tissue Formation, Ann. Otol., Rhin. & Laryng. **39**:533-541, 1930.

In general, three types of plastic operation have been described: formation of a flap from the palate, formation of a flap from the cheek and a combination of palatal and buccal flaps.

Welty [8] recommended the use of a palatal flap for the closure of the fistulous tract. Maybaum [9] and Dean [10] both advocated removal of part of the lingual and buccal plates of the alveolus about the fistula so that the flaps formed on the lingual and buccal aspects could be readily brought together and sutured. Vorhees [11] dissected a palatal flap as far as the midline, raised a flap from the cheek so as to get as much relaxation as possible and sutured the two flaps together. Zange [12] employed a somewhat similar procedure, tucking in the stump of the fistulous tract like the inverted stump of an appendix, and covered the raw area with alveolar and palatal flaps, like sliding doors. Dunning [13] mobilized palatal and buccal flaps, the palatal flap being hook shaped. As the palate flap is drawn toward the buccal flap, a small raw area is created on the hard palate, which is permitted to fill in by granulation.

Of the buccal flaps, that of Axhausen [14] is probably the most popular. In his procedure an area about the orifice of the fistula is denuded of epithelium, and a flap is raised from the cheek at a posterior level, rotated 90 degrees on its base and sutured to the denuded region. Pais [15] advocated closure by formation of buccal flaps in such a manner that they are sutured as a horizontal T. Fleischmann,[16] after excision of the scar and fistulous tract, closed the opening with a buccal flap, left attached at either end. Claoué [17] employed the lining of the fistulous

8. Welty, cited by Guthrie, D.: The Operative Closure of Oro-Maxillary Fistula, J. Laryng. & Otol. **47**:459-463, 1932; The Operative Closure of Oro-Maxillary Fistulae, Proc. Roy. Soc. Med. **25**:1063-1064, 1932.

9. Maybaum, J. L.: Two Cases of Empyema of the Maxillary Sinus of Dental Origin; Alveolar Fistula; Radical and Plastic Operation, Ann. Otol., Rhin. & Laryng. **32**:273-276, 1923.

10. Dean, L. W.: A Method of Closing a Sinus Between the Antrum of Highmore and the Mouth, J. A. M. A. **61**:1613-1614 (Nov. 1) 1913.

11. Vorhees, I. W.: Bucco-Antral Fistula: Closure by Plastic Procedure, Laryngoscope **37**:431-432, 1927.

12. Zange, J.: Zum plastischen Verschlusse von Kieferhöhlenmundfisteln, Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres **23**:685-692, 1926.

13. Dunning, H. S.: Maxillary Sinusitis of Oral Origin, Laryngoscope **35**: 766-771, 1925.

14. Axhausen, G.: Ueber den plastischen Verschluss von Antrum-Mundhöhlen Verbindungen, Deutsche Monatschr. f. Zahnh. **48**:193-204, 1930.

15. Pais, C.: Fistola alveolare del seno mascellare con mucocele suppurato, Valsalva **11**:217-221, 1935.

16. Fleischmann, O.: Ein einfaches Verfahren zum plastischen Verschluss von Kieferhöhlenmundfisteln, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **117**:306-308, 1928.

17. Claoué, C.: Fermeture d'une fistule du sinus maxillaire dans la fosse canine, J. de méd. de Bordeaux **106**:178-179, 1929.

tract to reconstruct the lining of the sinus. He turned down a flap of mucosa from the cheek and sutured it over the external opening. Frenzel [18] also employed a circular flap from the cheek to occlude the opening. New [19] advocated the principle of delayed buccal flap, allowing a week to elapse after elevation of the flap before transferring it to the fistulous site.

DESCRIPTION OF OPERATION

After completing the Denker operation (or the Caldwell-Luc) the plastic closure of the fistulous tract is next effected. Ordinarily this is done at the same time as the operation on the sinus.

The first step is to make a U-shaped incision about the fistulous opening, the limbs of the U being about 1 cm. from the fistulous opening

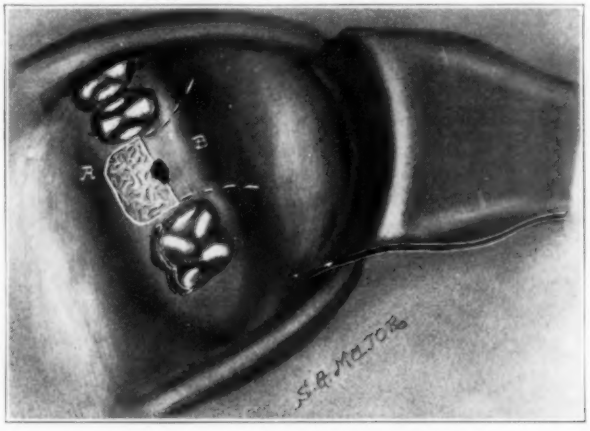

Fig. 1.—*A*, denuded area to which the plastic flap will be sutured. *B*, region in which the flap is to be formed.

on all sides, if conditions will permit, according to the presence or the absence of adjacent teeth (fig. 1). This incision is superficial and extends through the mucous membrane but not through the submucosa. An incision is next made at the level of the orifice of the fistula and parallel with the alveolus, extending from before backward, this incision being carried down to the bone and joining the limbs of the U. Within the confines of the U thus created the epithelium is removed with a sharp scalpel, so that a raw area will be formed. Later the flap will be sutured to this area. The fistulous tract is now cored out in the usual manner, care being taken that the lining is completely removed. To the

18. Frenzel, H.: Klapplappenplastik zum Verschluss von Kieferhöhlenmundfisteln, Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres **27**:509-513, 1929.

19. New, G. B.: The Use of the Delayed Flap in Secondary Operations on the Palate and Antrum, Minnesota Med. **6**:214-220, 1923.

buccal end of the U-shaped area a flap is now formed. Fine silk traction sutures are placed at either angle of the proposed flap, and incisions are carried down and outward toward the cheek, diverging as they proceed down into the buccal fold, a more adequate blood supply to the flap being thereby insured. These incisions are carried into the

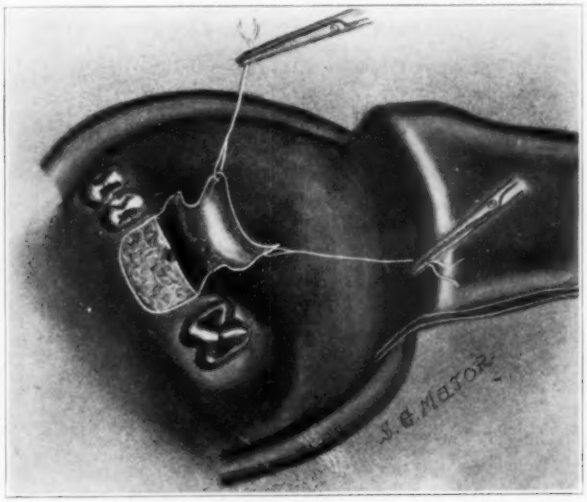

Fig. 2.—Elevation of the flap from the buccal sulcus.

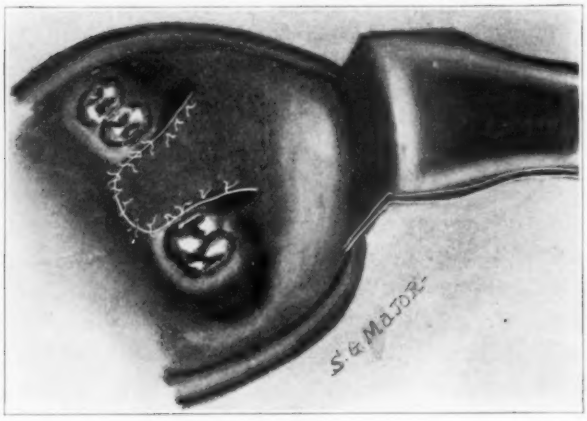

Fig. 3.—Flap sutured to the denuded area.

depth of the buccal fold and then outward onto the cheek. Rarely are they carried into the vicinity of the parotid duct, but this structure must be borne in mind and the dissection kept as remote from it as possible. The flap is now elevated from its bed, care being taken that

an adequate thickness is maintained. In the immediate vicinity of the fistulous opening the flap comprises the entire thickness of the mucoperiosteum, and as the dissection is carried down into the buccal sulcus and out onto the cheek the thickness is increased slightly as the dissection progresses. In this manner, taking advantage of the depth of the buccal sulcus, one may form a flap which may be opposed over the raw area to the lingual side of the orifice of the fistula with absolutely no tension and with an excellent blood supply (fig. 2).

By means of the traction sutures, the flap is now opposed over the previously prepared denuded area, where it is sutured with interrupted silk sutures, a fine round needle being used. My associates and I have found that a needle with a cutting edge is distinctly contraindicated for this purpose. Thus apposition of raw surface to raw surface is achieved instead of edge to edge approximation (fig. 3).

The postoperative care of the patients is like that after any oral plastic operation. The silk sutures are ordinarily removed on the eighth postoperative day.

COMMENT

The principle of surface to surface instead of edge to edge approximation is a meritorius one. My associates and I have found the blood supply of these flaps to be excellent and have seldom resorted to delayed flaps. The operation has been performed on 23 patients, with primary closure in 21 cases. In the other 2 cases it was felt that the results were unsatisfactory because of excessive scarring about the orifice of the fistula. At a second operation in both these cases closure was accomplished without difficulty.

It is well to caution the patient against excessive mastication or talking during the ten days following the operation, since these acts exert stress on the base of the flap. We have not found it necessary to wire the teeth to accomplish this purpose. Rarely is it necessary subsequently to detach the base of the flap from the cheek.

SUMMARY

The general factors in the causation of buccoantral fistulas have been discussed, together with a plastic method of closure.

ROENTGENOLOGIC STUDY OF THE HYPOPHARYNX, LARYNX AND TRACHEA

ITS USE IN LARYNGEAL DIAGNOSIS

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MILWAUKEE

The use of roentgenography as an aid in diagnosis of diseases of the hypopharynx, larynx, trachea and soft tissues of the neck is of great importance in many cases, particularly when complications of the mediastinum or lungs may exist. A systematic roentgenologic study of the entire respiratory tract is advisable for all patients with laryngeal involvement.

Since the pioneer work of Samuel Iglauer,[1] 1914, there has been comparatively little roentgenologic study of the soft tissues of the neck by the laryngologist. Brown [2] stated that this also holds true for the roentgenologist. However, a number of excellent papers have been written during the past five years by roentgenologists, notably by Hay,[3] Pancoast,[4] Pendergrass,[5] Brown, and Coutard and Baclesse.[6] The last-mentioned authors presented a large number of cases studied roentgenologically during the course of roentgenotherapy of epithelioma of the larynx and hypopharynx.

A thorough roentgenologic study of the larynx and trachea was made for a number of patients in whose cases a diagnosis was exceedingly difficult. I refer especially to a patient in whose case no reason for what appeared to be severe localized laryngitis could be determined.

Presented as a candidate's thesis to the American Laryngological, Rhinological and Otological Society, Inc.

1. Iglauer, S.: Value of Roentgenography in the Diagnosis of Diseases of the Larynx and Trachea, J. A. M. A. **63**:1827-1831 (Nov. 21) 1914.

2. Brown, S., and Reinecke, H. G.: Roentgenological Study of the Neck, Am. J. Roentgenol. **20**:208-212 (Sept.) 1928.

3. Hay, P. D.: The Neck Roentgenologically Considered, New York, Paul B. Hoeber, Inc., 1929.

4. Pancoast, H. K.: Roentgenology of the Upper Respiratory Tract, J. A. M. A. **95**:1318-1321 (Nov. 1) 1930.

5. Pendergrass, E. P.: The Value of Roentgen Diagnosis in Diseases of the Neck and Upper Respiratory Tract, Kansas City Southwest Clin. Soc. Monthly Bull. **7**:18-22 (April) 1931.

6. Coutard, H., and Baclesse, F.: Roentgen Diagnosis During the Course of Roentgen Therapy of Epitheliomas of the Larynx and Hypopharynx, Am. J. Roentgenol. **28**:293-312 (Sept.) 1932.

The soft tissues immediately above the vocal cords were edematous, and the swelling appeared to be limited to that area within the larynx. Clinical and roentgenologic examinations of the chest gave negative results; hence it was decided to take several pictures of the soft tissues of the neck, and what seemed to be a definite breaking down or erosion of the thyroid cartilage was found.

Pancoast, however, stated that one is not justified in interpreting a condition as erosion unless the adjacent soft tissues are swollen and hazy.

Subsequent to the study of the case just described, a systematic roentgenologic study of the larynx and the entire respiratory tract has become a routine procedure for all patients with laryngeal involvement.

Pendergrass stated that roentgen examinations offer a permanent record of the location and extent of the disease or growth, just as a microscopic slide becomes a permanent record of the pathologic process. For children, according to Pancoast and Pendergrass,[7] a complete roentgenologic examination of the entire respiratory tract should always be made. When irradiation is the form of treatment, frequent roentgenograms definitely record the progression or regression of the lesion, especially in cases of carcinoma.

Pancoast uses fluoroscopy as a first procedure in all examinations of the neck. Fluoroscopy is used for study of the moving parts and roentgenography for the recording of the finer details. A general survey of the region is first made; then the patient is directed to produce certain vowel sounds and the appearance of the ventricles is noted. If the larynx is normal, the air-containing, zeppelin-shaped cavity of the ventricles is clearly defined. Pancoast continues with the observation of the arytenoid cartilages, the lumen of the pharynx, the piriform sinuses, the vestibule of the larynx and the trachea. This examination is followed by a study of the swallowing mechanism to determine the integrity of the motor mechanism of the pharynx, larynx and upper part of the esophagus.

From the references of Thost,[8] Iglauer, Pancoast,[9] Coutard and Baclesse, Kohler[10] and Pack and Craver,[11] the following outline has

7. Pancoast, H. K., and Pendergrass, E. P.: Roentgenological Diagnosis of Diseases of the Upper Respiratory Tract in Children, Am. J. Roentgenol. **23**: 241-264 (March) 1930.

8. Thost, A.: Archiv und Atlas des normalen und kranken Kehlkopfs des Lebenden im Röntgenbild, Fortschr. a. d. Geb. d. Röntgenstrahlen, 1913, supp. 31.

9. Pancoast, H. K.: Roentgenology of the Pharynx and Upper Esophagus, Am. J. Cancer **17**:373-395 (Feb.) 1933.

10. Kohler, A.: Roentgenology, Baltimore, William Wood & Company, 1935.

11. Pack, G. T., and Craver, L. F.: Tumors of the Larynx and Thyroid: A Roentgenographic Study, Arch. Otolaryng. **13**:658-675 (May) 1931.

been arranged in order to obtain a clear conception of the normal and the abnormal changes in the larynx:

1. Roentgenography of the normal larynx and hypopharynx.

2. Pathologic changes in the roentgenographic appearance of the larynx, hypopharynx and trachea.

NORMAL LARYNX

Normally the larynx and hypopharynx present clear shadows and transparent areas, with well defined, easily demonstrated contours (fig. 1). There are four essential points to be considered in the examination of the normal larynx and hypopharynx: the osteocartilaginous frame work, the shadows, the transparent areas and the relations of these various parts to each other (Coutard and Baclesse). The roentgenogram of the normal larynx (Iglauer and Pancoast) reveals the

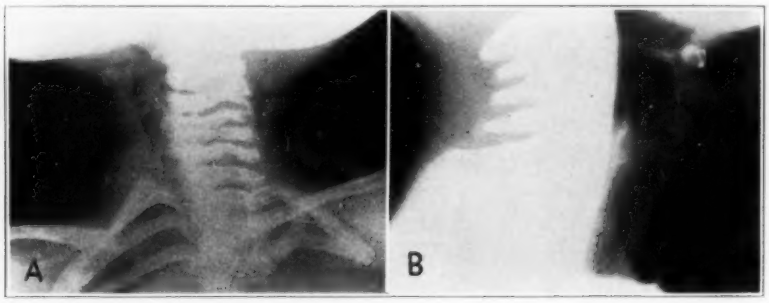

Fig. 1.—*A*, normal larynx of a child aged 6 years. *B*, normal larynx of an adult.

following structures: the soft palate, the pharynx, the posterior border of the tongue and the horseshoe-shaped hyoid bone, with its two processes sharply defined. The epiglottis can be seen projecting between the wings of the hyoid bone. The thyroid cartilage may be more or less ossified and prominent, while the cricoid cartilage is covered somewhat by the descending horns of the thyroid. The ventricles, the ventricular bands and the vocal cords can be seen. The arytenoids, the aryepiglottic folds and the cricothyroid space can be distinguished. The lumen of the larynx appears distinctly as a lighter area in the photographic print but dark in the roentgenogram and is continuous below with the well defined lumen of the trachea. The cartilaginous rings of the trachea are evident, especially when ossification has taken place. All paired structures are superimposed.

Roentgenograms are particularly valuable for the study of the normal process of ossification of the laryngeal cartilages. In order to appreciate the pathologic changes in these structures one should be familiar

with the usual course of ossification. This is a true metaplasia of cartilage into bone (Chamberlain and Young [12]). Ossification usually begins (Fraenkel [13]) during the eighteenth or nineteenth year of life, at the lower part of the posterior border. There the ossification extends forward along the inferior border of the thyroid, presenting an L-shaped mass of bone. Iglauer has covered this subject in his paper.

CARCINOMA

Carcinoma of the larynx is usually found in the ossified larynx of the aged (fig. 2). When epithelioma develops, the changes in the roentgen appearance (Coutard and Baclesse) of the larynx and hypopharynx are as follows: the projection of a dense shadow over a normally transparent clear space without the distortion of the normal segments and spaces. This, they contended, is the simplest diagnostic point to indicate the presence of a fungating tumor. A distortion of the normal segments and spaces indicates a complicated infiltrating tumor or a simple epithelioma of considerable size. Pancoast stated that there are five appearances by which a neoplasm of the larynx may be recognized:

1. Direct evidence of a localized nodule in the air space of the vestibule, ventricles or subglottic region. A benign tumor is usually cleancut in outline and distinctly localized, while a malignant tumor is hazy and fades off gradually into surrounding tissues, there being an infiltration edema or inflammatory reaction.

2. Obliteration of the ventricles, due to a growth or to paralysis of the vocal cord.

3. Irregularity or change in the direction of the normally cleancut horizontal line at the lower border of the larynx.

4. Complex changes in the appearance, due to extensive growth, i. e., destruction of tissue, distortion and displacement.

5. Infiltration of cartilage, which, however, cannot be definitely determined.

TUBERCULOSIS

Characteristic of tuberculosis, according to Iglauer, is a roentgenogram in which there is a peculiar hazy, indistinct outline of the laryngeal cartilages and which presents the impression of an overexposed picture (fig. 3). This roentgen finding, he maintained, is of diagnostic value, as it reveals the fact that the tuberculous process is not confined to the lining membranes but invades the underlying cartilage also, asso-

12. Chamberlain, W. E., and Young, R. R.: Ossification (So-Called "Calcification") of Normal Laryngeal Cartilages Mistaken for Foreign Body, Am. J. Roentgenol. **33**:441-450 (April) 1935.

13. Fraenkel, E.: Ueber die Verknocherung des menschlichen Kehlkopfs, Fortschr. a. d. Geb. d. Röntgenstrahlen **12**:152-168, 1908.

ciated with the resorption of bone. It is analogous to rarefying changes noted in roentgenograms of the long bones and joints when tuberculosis is found. There occurs also an infiltration of the soft parts, and the aryepiglottic folds are distinctly presented.

Tuberculosis, according to Pendergrass, frequently involves the arytenoids, and in swallowing food may spill into the larynx instead of going into the esophagus.

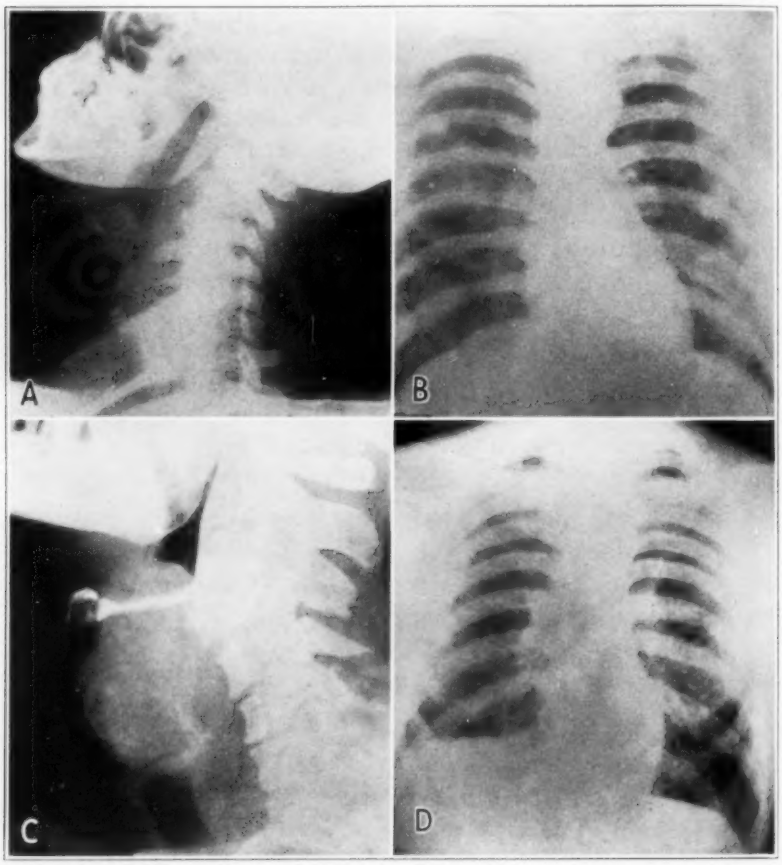

Fig. 2.—*A*, extensive carcinoma of the larynx. *B*, diffuse metastases in the lungs of the same patient as in *A*, *C*, extensive carcinoma of the larynx. *D*, chest of the same patient as in *C*, showing silicosis.

SYPHILIS

Iglauer stated that when tertiary syphilis of the larynx is present the roentgenogram shows a tendency to proliferation rather than resorption of bone, which occurs in tuberculosis (fig. 4). He maintained, therefore, that roentgenography could be used to differentiate syphilis from tuberculosis. Pendergrass, however, said that syphilis cannot be

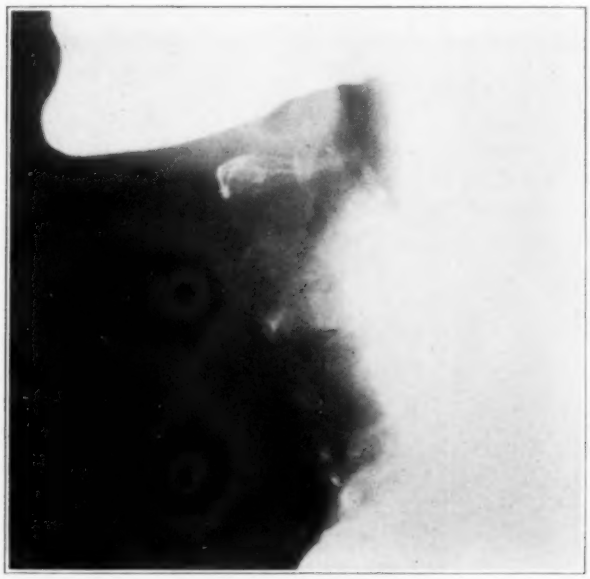

Fig. 3.—Tuberculosis of the larynx.

Fig. 4.—Syphilis of the larynx. The epiglottis has been completely destroyed by an ulcerative gumma.

differentiated roentgenologically from tuberculosis. On the basis of my studies I feel that this differentiation can be made roentgenologically.

PARALYSIS OF THE VOCAL CORDS

In cases of paralysis of the vocal cords, Pancoast stated, there is practically always a change in the appearance of the ventricles (fig. 5).

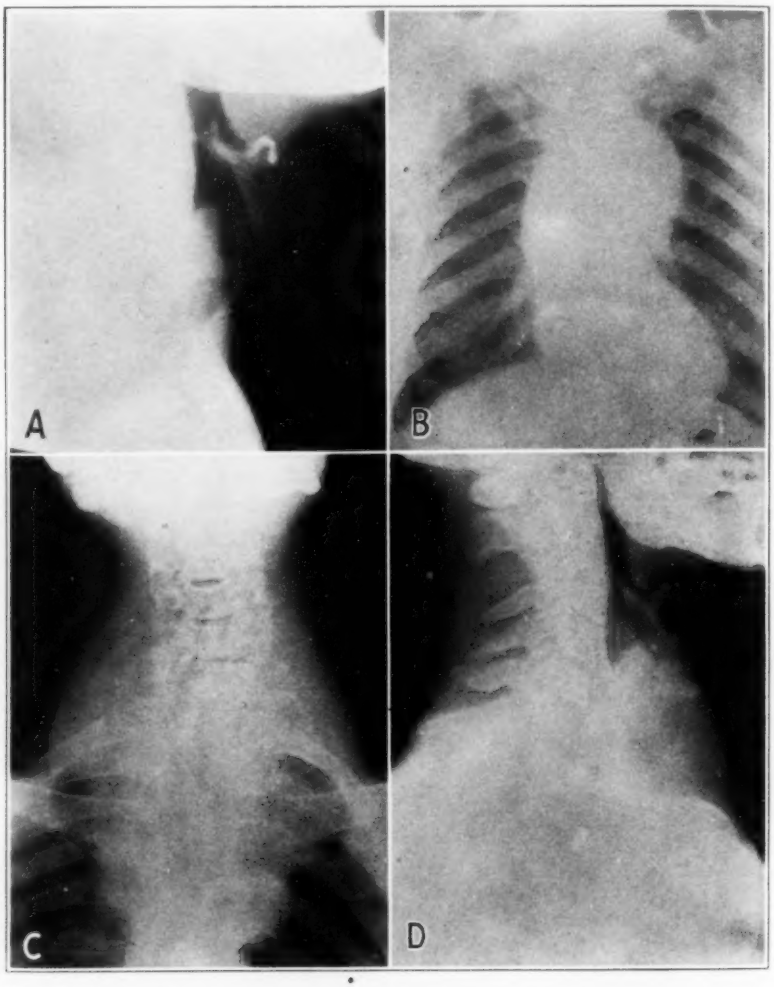

Fig. 5.—*A*, paralysis of the vocal cord; *B*, aneurysm, same patient as in *A*; *C* and *D*, large goiter extending below the sternum.

1. There are variations in the zeppelin shape of the ventricle, the lower half of which may be eliminated entirely. A similar appearance may also be seen in normal persons when the cricoid cartilage is dense; however, the half-space is then wider than when the cord is paralyzed.

2. The zeppelin shape can be seen, but the posterior half of the space is closed on one side by a contraction upward of the lower part of the posterior portion. The borders of the space are cleancut, not hazy as when the deformity is due to a growth.

3. When complete obliteration of the space occurs, the appearance of a growth cannot be differentiated from that of an inflammatory condition. (No attempt has been made in this paper to enter into a roentgenologic discussion of the acute inflammatory conditions occurring in the soft tissues of the neck.)

TECHNIC

The method employed is that suggested by Pancoast and Hickey,[14] in that the exposure is timed during the phonation of a vowel. The ventricles can be best shown by having the patient say Ā. Hickey recommended flash exposures to prevent blurring, which might occur from movement of the laryngeal structures or possibly from cardiac impact, during a slow exposure. If a second film is desired, showing the laryngeal structures at rest, it is essential to warn the patient not to swallow during the exposure. Overexposures should be guarded against. The kilovoltage should be kept as low as possible in order to secure the maximum contrast in the soft tissues. In other words, a film of the desired density is one which would be considered underexposed in a study of the cervical portion of the spine; or again a lateral film of the neck with proper exposure to demonstrate the cervical vertebrae would be overexposed for laryngeal diagnosis. The technic used is as follows: kilovolts 65, milliamperage 50, focal distance 60 inches (152 cm.), time one-fourth to one-half second.

CONCLUSIONS AND SUMMARY

1. The roentgenographic examination of bone in otolaryngology is in universal practice, but the value of such examination of soft tissues is generally not appreciated.

2. Not infrequently, conclusive information may be obtained from roentgenograms of the larynx in the diagnosis of syphilis, tuberculosis, neoplasms, paralysis of the vocal cord and various types of stenoses.

3. Roentgenographic study is of especial value and importance when indirect or direct complete inspection of the larynx is difficult or impossible.

4. Definition of a neoplasm and the extent of its gross infiltration into extralaryngeal tissue may be determined by roentgenographic examination.

5. The technic is that ordinarily used in examining soft tissue and is within the scope of the average competent roentgenologist. With experience and study, the interpretation of the roentgen evidence is relatively simple.

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14. Hickey, P. M.: Radiography of Normal Larynx, Radiology **11**:409, 1928.

SULFANILAMIDE THERAPY FOR ACUTE OTITIS MEDIA AND ACUTE MASTOIDITIS

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The use of sulfanilamide as a chemotherapeutic agent in the treatment of acute infections of the ear is being acclaimed by groups everywhere.[1] The reports of successful treatment in cases of hemolytic streptococcic septicemia and of meningitis are increasing at a rapid rate. The drug now has an established place in the therapy of these complications. The evaluation of sulfanilamide therapy in all cases of otitis media or mastoiditis requires an enormous amount of clinical application. Several questions have arisen since the drug was introduced. Should every patient who has acute otitis media receive sulfanilamide? Is there less need for surgical intervention in cases of acute mastoiditis? What is the clinical course of a patient receiving the drug?

This study includes reports on 21 patients with acute otitis media or acute mastoiditis treated in the Babies Hospital from December 1937 to April 1938 and on 1 patient treated in the Presbyterian Hospital. The reports of 2 cases of meningitis and 1 case of septicemia, in all of which the disease was of otitic origin, are included.

The ages of the patients ranged between 4 months and 12 years, with one exception, a 17 year old boy.

Marshall, Emerson and Cutting[2] found that after a single dose of the drug the level of sulfanilamide in the blood reached its peak within three to four hours. After this period, the level in the blood fell, and the major part of the drug was found to have been excreted at the end of twenty-four hours. The concentration of the drug in

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1. (*a*) Proceedings of the Chicago Laryngological and Otological Society, Ann. Otol., Rhin. & Laryng. **46**:1124 (Dec.) 1937. (*b*) Flake, C. G., and Carey, B. J.: Para-Amino-Benzene-Sulfonamide and Its Derivatives in the Treatment of Beta-Hemolytic Streptococcus Infections of the Middle Ear and Mastoid, New England J. Med. **217**:1033 (Dec. 23) 1937.

2. Marshall, E. K., Jr.; Emerson, K., Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide: Absorption and Excretion; Method of Determination in Urine and Blood, J. A. M. A. **108**:953 (March 20) 1937.

the spinal fluid was only slightly lower than that in the blood within a few hours after administration by mouth. They stated also that the concentration of the drug in the tissues is dependent on the concentration in the blood. Marshall, Cutting and Emerson [3] and Fuller [4] have worked out methods for determining the amount of the drug in the blood, spinal fluid and urine. Long and Bliss [5] stated that it is necessary to reach a high level in the blood as quickly as possible to secure the best results. They administer a large initial dose with the aim of attaining a level of 10 mg. per hundred cubic centimeters in the blood in four hours. After this period they give the patient smaller doses, which must be adequate to keep the concentration in the blood at this level.

The toxic manifestations of the drug have been reported by other observers.[6] Long and Bliss [7] advised against the use of saline laxatives during sulfanilamide therapy. The response of the blood cells to the drug has been reported by Bigler.[8]

The sulfanilamide in our cases was administered by the department of pediatrics. The dose was based on body weight. An average of about 0.1 Gm. per kilogram of body weight was given daily, divided into four doses. The drug in many instances was given subcutaneously. The solution used contained 0.8 Gm. per hundred cubic centimeters of sterile physiologic solution of sodium chloride. The same preparation was also used intrathecally.

There were no fatalities attributable to the drug. The toxic symptoms that developed in our group were not severe. Cyanosis occurred frequently and was not regarded as an indication to discontinue treat-

3. Marshall, E. K., Jr.; Cutting, W. C., and Emerson, K., Jr.: Acetylation of Para-Aminobenzenesulfonamide in the Animal Organism, Science **85**:202 (Feb. 19) 1937.

4. Fuller, A. T.: Is Para-Aminobenzenesulphonamide the Active Agent in Prontosil Therapy? Lancet **1**:194 (Jan. 23) 1937.

5. Long, P. H., and Bliss, E. A.: The Use of Para-Aminobenzenesulphonamide (Sulfanilamide) or Its Derivatives in the Treatment of Infections Due to Beta-Hemolytic Streptococci, Pneumococci, and Meningococci, South. M. J. **30**: 479 (May) 1937.

6. Long, P. H., and Bliss, E. A.: The Clinical Use of Sulfanilamide and Its Derivatives in the Treatment of Infectious Diseases, Ann. Int. Med. **11**:575 (Oct.) 1937. Schnitzker, M. A.: Sulfanilamide: A Review, New England J. Med. **218**:503 (March 24) 1938.

7. Long, P. H., and Bliss, E. A.: Para-Aminobenzenesulfonamide and Its Derivatives: Experimental and Clinical Observations on Their Use in the Treatment of Beta-Hemolytic Streptococcic Infection; Preliminary Report, J. A. M. A. **108**:32 (Jan. 2) 1937.

8. Bigler, J. A.: Blood Cell Response to Sulfanilamide Therapy, Ann. Otol., Rhin. & Laryng. **47**:219 (March) 1938.

Cases of Acute Otitis Media and Acute Mastoiditis

Case	Sex	Age	Diagnosis on Admission	Temperature on Admission, F.	Organism	Mastoid Involvement	Sulfanilamide	Result
1. L. C.	M	5½ mo.	Acute purulent otitis media, right side, of 2 days' duration	102	Str. haemolyticus	None	12.6 Gm. in 6 days	Ear dry 5 days after admission; patient has remained well
2. R. H.	M	6 yr.	Acute purulent otitis media, bilateral, of 2 days' duration	102	Str. haemolyticus, bilateral	Bilateral mastoid tenderness	6 Gm. in 3 days	Ears dry on second day of sulfanilamide therapy; patient has remained well
3. R. T.	M	2 yr.	Acute purulent otitis media, right side (developed in hospital)	102	Str. haemolyticus	Extensive destruction of bone; surgical mastoiditis	14.7 Gm. in 11 days	Ear dry on 19th day; patient remained well for 1 month
R. T.	M	2 yr.	Pneumonia and acute purulent otitis media, bilateral, 1 mo. after previous admission	105.4	Pneumococcus type III, bilateral	Extensive destruction of right mastoid; cloudiness of left mastoid	3.9 Gm. in 5 days	Right ear dry in 1 day; left ear dry in 1 week; patient has remained well
4. D. M.	M	8 yr.	Acute purulent otitis media, right side, of 1 day's duration	101	Str. haemolyticus	Mastoid tenderness and cloudiness	20.6 Gm. in 7 days	Ear dry on 12th day; symptoms disappeared immediately; patient has remained well
5. E. B.	F	7 yr.	Acute purulent otitis media, right side, of 8 days' duration	103	Str. haemolyticus	None except roentgenographic cloudiness	13.8 Gm. in 6 days	Ear dry on 3d day; patient has remained well
6. M. B.	F	7 yr.	Acute purulent otitis media, left side, of 3 days' duration	101	Str. haemolyticus	Roentgenologic and clinical evidence of mastoiditis	11.7 Gm. in 4 days	Ear dry in 4 days; patient has remained well
7. D. B.	M	4 yr.	Acute purulent otitis media, right side, of 9 days' duration	99	Str. haemolyticus	Roentgenologic evidence of mastoiditis; mastoid tenderness	10.8 Gm. in 6 adys	Ear became dry promptly; patient has remained well
8. M. T.	M	12 yr.	Acute purulent otitis media, left side, and acute mastoiditis of 6 days' duration	104.4	Str. haemolyticus, in blood stream	Roentgenologic evidence of mastoiditis; destruction of bone; mastoid tenderness; surgical mastoiditis	26.7 Gm. in 8 days	Acute mastoiditis and septicemia; patient recovered (see case reports)
9. W. H.	M	12 yr.	Acute purulent otitis media, bilateral, of 5 days' duration	104	Str. haemolyticus, bilateral	None	28.8 Gm. in 8 days	Ears dry on 8th day; patient has remained well
10. J. W.	M	7 yr.	Recurrent mastoiditis, right; meningitis	104	Str. haemolyticus, in ear and spinal fluid	Recurrent mastoiditis	81.15 Gm. in 56 days	Operation (see case reports)
11. P. C.	M	17 yr.	Acute purulent otitis media, left side, of 2 weeks' duration; meningitis	104.4	Str. haemolyticus, in ear and spinal fluid	None	76 Gm. in 22 days	Operation (see case reports)

tion; meningitis

12. H. R.	F	3 yr.	Acute purulent otitis media, left side, of 3 weeks' duration	100	Str. haemolyticus; hemolytic Staph. aureus	None	12.3 Gm. in 5 days	Ear dry on 3d day; patient has remained well
13. H. H.	M	1 yr.	Bronchopneumonia; acute purulent otitis media, left side (developed in hospital)	102	Str. haemolyticus; hemolytic Staph. aureus	None	18.15 Gm. in 15 days	Ear continued to discharge for 27 days; no effect from sulfanilamide
14. P. G.	F	3 yr.	Acute purulent otitis media, left side, of 10 days' duration	102	Str. haemolyticus; Staph. albus	Roentgenologic evidence of mastoiditis; complete breaking down; mastoid tenderness	10.8 Gm. in 6 days	Sulfanilamide had no effect; mastoidectomy performed
15. C. A.	F	1 yr.	Acute purulent otitis media, bilateral, of 2 weeks' duration	98.6	Str. haemolytigus; hemolytic Staph. aureus	None	5.6 Gm. in 4 days	Both ears dry in 2 days; patient has remained well
16. N. B.	F	6 yr.	Acute purulent otitis media, left side, of 3 weeks' duration	101	Str. haemolyticus; hemolytic Staph. aureus	Tenderness; sagging of wall of canal; roentgenologic evidence of mastoiditis; destruction of bone	16.2 Gm. in 5 days	Mastoidectomy performed; cultures at operation revealed no growth
17. N. J.	F	22 mo.	Acute purulent otitis media, bilateral, of 20 days' duration	100	Str. haemolyticus; hemolytic Staph. aureus; B. influenzae	None	20.4 Gm. in 16 days	Sulfanilamide probably was of benefit; ears became dry
N. J.	F	22 mo.	Acute purulent otitis media, right side, 4 days after discharge	102	Str. haemolyticus; hemolytic Staph. aureus; B. influenzae	None	13.8 Gm. in 7 days	Right ear dry on 5th day; patient has remained well
18. M. H.	F	5 yr.	Acute purulent otitis media, right side, of 18 days' duration	100	Str. haemolyticus; hemolytic Staph. aureus	Mastoid tenderness	8.4 Gm. in 6 days	Ear dry on 4th day; patient has remained well
19. J. T.	M	4 yr.	Acute purulent otitis media, bilateral, of 3 weeks' duration	100	Str. haemolyticus; hemolytic Staph. aureus, bilateral	Mastoid tenderness; roentgenologic evidence of mastoiditis; cloudiness	24.6 Gm. in 16 days	No effect from sulfanilamide; ears continued to discharge
20. M. N.	M	4 yr.	Acute purulent otitis media, bilateral, of 4 days' duration	101	Str. haemolyticus; hemolytic Staph. aureus, bilateral	None	16.8 Gm. in 9 days	Ears became dry; sulfanilamide probably helped
21. P. W.	M	7 yr.	Acute purulent otitis media, left side, of 2 day's duration	102.5	Pneumococcus type III	Mastoid tenderness; roentgenologic evidence of mastoiditis	25.8 Gm. in 8 days	Ear dry in 5 days; patient has remained well
22. R. S.	M	4 mo.	Acute purulent otitis media, bilateral; meningitis and septicemia	102	B. acidi lactici, in ears, blood and spinal fluid	None	18 Gm. in 11 days	Death

ment. The anemia which developed in our patients was treated by blood transfusion.

The cases recorded in the table are those in which sulfanilamide was given a fair trial. An attempt was made to secure the full benefits of the drug before resorting to other methods of otologic practice.

ORGANISMS

Streptococcus haemolyticus was the sole infective agent in 11 cases. All of the patients recovered from the infections. In 4 of the cases a diagnosis of surgical mastoiditis was made and one of these patients had bacteremia, but surgical intervention was not necessary. The duration of the illness before treatment was two to fourteen days. It took an average of seven and two-tenths days for the ears to become dry. Two patients of this group had meningitis on admission, and mastoidectomy was performed immediately and sulfanilamide then given. The cases will be reported later in this paper.

Sulfanilamide acts best in hemolytic streptococcic infections.[7] The results obtained in our group of patients were in agreement with this fact, and all the patients with this type of infection responded well. There is a tendency for streptococcic infections to recur; the drug should therefore be continued until the patient is well on the way to recovery.

Str. haemolyticus and Staphylococcus aureus or albus were combined in 9 cases. Six patients were well in from two to fifteen days. In the other 3 instances there was no demonstrable beneficial effect from the sulfanilamide.

Meleney[9] uses sulfanilamide by oral administration and staphylococcic bacteriophage locally in the treatment of combined hemolytic streptococcic and staphylococcic infections elsewhere in the body. His results have been good. This combination may be of value in treating acute otitis media due to a combined infection.

One patient infected with Pneumococcus type III, with evidence of mastoiditis, had dry ears after four days of sulfanilamide therapy. In 1 of the patients who had recovered from mastoiditis due to Str. haemolyticus, an infection of the same ear developed with Pneumococcus type III one month after discharge from the hospital. This infection responded to sulfanilamide therapy, and the ear became dry in one week.

Rosenthal, Bauer and Branham[10] found after considerable experimental work that they were unable to obtain compounds more effective than sulfanilamide against pneumococcic infections.

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9. Meleney, F. L.: Personal communication to the authors.

10. Rosenthal, S. M.; Bauer, J., and Branham, S. H.: Comparative Studies of Sulfanilamide Compounds in Experimental Pneumococcus, Streptococcus and Meningococcus Infections, Pub. Health Rep. **52**:662 (May 21) 1937.

CLINICAL OBSERVATIONS

The person with toxic symptoms, high temperature and mastoid tenderness, with a history of a discharging ear of from a few days' to a week's duration, gave the best response to sulfanilamide therapy. The temperature would frequently become normal within twenty-four hours, and the toxic symptoms as well as mastoid tenderness would disappear.

Occasionally the middle ear would become dry within a few days, but more often the ear continued to discharge for a longer period, while the patient remained free of symptoms.

The development of fever in our patients receiving sulfanilamide was not uncommon. It usually occurred after the drug had been administered for several days. The temperature would be normal, and then daily fluctuations from 101 to 104 F. would occur. When such a case was encountered, it gave considerable concern, particularly if the patient had mastoiditis. The possibility of a complication, such as sinus thrombosis or meningitis, was brought to mind. Removal of the drug in such instances was followed by a return of the temperature to normal within seventy-two hours. The patient with fever due to sulfanilamide usually has a rash but otherwise presents no alarming symptoms.

REPORT OF CASES

One case of septicemia and 2 cases of meningitis of otitic origin are reported.

CASE 8.—M. T., a white boy 12 years of age, was admitted to the Babies Hospital with a history of a discharging ear of six days' duration.

History.—The patient had had no previous infections of the ear. A myringotomy had been performed in the outpatient department at the start of the illness, and he had been observed daily until the day of admission. When he was admitted to the hospital his temperature was 104.2 F., and he complained of severe pain in the left side of his head.

Examination.—Except for the presence of acute rhinitis and acute otitis media of the left ear, the findings were essentially normal.

The left external auditory canal was filled with a thin purulent discharge. The left drum had a large opening in the posterior inferior quadrant, and the drum itself was thick and red. There was definite mastoid tenderness.

The blood count was: hemoglobin, 14.5 Gm. per hundred cubic centimeters; red cells, 6,000,000; white cells, 24,000; polymorphonuclears, 91 per cent.

A roentgen examination by Dr. J. Caffey was reported as showing the following picture:

"In the left temporal bone there are a marked reduction in the air content and almost complete loss of definition of the cellular structure. The shadow superimposed over the lateral sinus shows practically complete absence of septal walls. The right temporal bone is normal.

"Impression: The findings on the left side are consistent with a large amount of inflammatory exudate throughout the pneumatized portion of the temporal bone and with a widespread demineralization of the septal walls, with complete absence of walls over the lateral sinus."

Course.—The day following admission to the hospital the patient's temperature rose to 106 F., and he became stuporous and complained of headache. Cultures of the discharge from the ear revealed Str. haemolyticus. A culture of the blood taken at the height of the temperature also showed the presence of Str. haemolyticus. The patient was given sulfanilamide, receiving 4.5 Gm. the first day after admission and 3.6 Gm. daily for the next six days. His temperature was at first elevated between 103 and 106 F., but it dropped to 100 F. forty-eight hours after the administration of sulfanilamide, and on the fifth day after admission it was normal. The discharge from the left middle ear decreased markedly, and the left middle ear was dry on the sixth day. The patient was discharged as well on the twelfth day. He had received 26.7 Gm. of sulfanilamide in eight days.

Comment.—This is a case of acute otitis media and acute mastoiditis with bacteremia due to Str. haemolyticus in which the patient received sulfanilamide and recovered from the infection without operation.

CASE 10.—J. W., a white boy 7 years of age, was admitted to the Babies Hospital on Feb. 23, 1938, with recurrent mastoiditis and a discharging postauricular wound of one month's duration.

History.—On Oct. 28, 1936, he was admitted to the Willard Parker Hospital with the diagnosis of scarlet fever. Bilateral mastoiditis and meningitis developed. The cultures of the spinal fluid and the discharge from the middle ear on both sides revealed the organism to be Str. haemolyticus. A bilateral mastoidectomy was performed. He was given convalescent scarlet fever serum, frequent blood transfusions and sulfanilamide and its derivatives. He made a complete recovery and was discharged from the hospital on Jan. 29, 1937. This case of otitic meningitis was reported in the literature by Woodman.[11]

The patient remained well until Jan. 20, 1938, at which time a right postauricular abscess developed during an acute infection of the upper part of the respiratory tract. The abscess was incised, and the wound was dressed daily. His condition was satisfactory until February 18, at which time he began to have transient headache. On February 23 his temperature rose to 104 F. and he complained of feeling dizzy on attempting to sit up in bed. He was admitted to the Babies Hospital.

Physical Examination.—He was apprehensive and pallid and complained of vertigo and right-sided headache. He preferred to lie on his right side.

The pupils of the eyes reacted normally. There was a fine nystagmus, most marked on upward left lateral gaze. The margins of the optic disk appeared to be slightly blurred.

The drum of the left ear was intact, and there was a well healed scar from the previous mastoidectomy.

The drum of the right ear was thick and red, and the right external auditory canal contained a scant amount of purulent discharge. There was an open postauricular wound with slight drainage.

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11. Woodman, DeG.: Otitic Meningitis, Arch. Otolaryng. **26**:310 (Sept.) 1937.

The mucous membrane of the nose was slightly congested.

There was definite rigidity of the neck.

The reflexes of the extremities were active. There was no Babinski sign. Kernig's sign was present bilaterally.

The remainder of the examination revealed nothing unusual.

Laboratory Findings.—The blood count was: hemoglobin, 13.6 Gm. per hundred cubic centimeters; red cells, 4,200,000; white cells, 22,350; polymorphonuclears, 79 per cent.

The spinal fluid was turbid and colorless. The initial pressure was 140 mm. There were 290 white blood cells per cubic millimeter, with 42 per cent polymorphonuclears and 58 per cent lymphocytes. Smears showed a few gram-positive chains of cocci. Culture produced no growth. Culture of the discharge from the middle ear revealed Str. haemolyticus.

Course.—Sulfanilamide therapy was started. The patient received 1.8 Gm. the first night and 3.9 Gm. the following day and thereafter was given smaller doses. He was seen by several members of the neurologic and neurosurgical services, and it was the consensus that he had meningitis. On February 24, the day after admission, he presented slight weakness of the lower half of the right side of the face and some weakness of the right half of the tongue. His headache was severe and not in any definite location. It was now thought that localizing signs of infection were developing in the right posterior fossa, and it was decided that a radical mastoidectomy on the right side should be performed. On February 25, Dr. De Graaf Woodman did the mastoidectomy, with the patient under general anesthesia.

A lumbar puncture just before operation showed that the spinal fluid was turbid and colorless, under an initial pressure of 160 mm., containing 250 white blood cells per cubic millimeter, with 58 per cent polymorphonuclears and 42 per cent lymphocytes. Smears showed a few gram-positive cocci in chains. A culture of Str. haemolyticus was grown.

At operation the mastoid cavity and middle ear were found to be filled with granulation tissue. The dural plate, which had been removed a year previously, was found to have almost completely regenerated. The dural and sinal plates were removed and the dura and sinus examined. There was no evidence of any localized infection. The dura was not under pressure and appeared to be normal. The posterior wound was left open at the completion of the operation. The patient was given a blood transfusion, and he returned to the ward in good condition.

The day after operation his condition seemed improved. The right facial weakness was less marked, but the headache, Kernig sign and rigidity of the neck persisted. A lumbar puncture was performed, with the following findings: The spinal fluid was turbid, under an initial pressure of 160 mm., containing 1,020 white blood cells per cubic millimeter, with 40 per cent polymorphonuclears and 60 per cent lymphocytes. No organisms were seen on smears. Cultures produced no growth.

On February 27, two days after operation, the headache was gone, and there was less rigidity of the neck.

A lumbar puncture was again done on February 28. The spinal fluid showed a slight cloudiness, had an initial pressure of 110 mm. and contained 320 white blood cells per cubic millimeter, with 60 per cent polymorphonuclears and 40 per cent lymphocytes. No organisms were seen on smears. Cultures produced no growth.

On March 2, his fifth postoperative day, the headache, rigidity of the neck and Kernig sign had disappeared. His mentality was clear, and his temperature was normal.

On March 10, recovery from the meningitis seemed complete. The posterior wound, which was left open at the time of operation, was closed, with the patient under general anesthesia. The mastoidectomy wound was slow in healing. Cultures from the wound showed the presence of Str. haemolyticus and Staph. aureus haemolyticus. Up to the time of writing there is still slight drainage, but the patient is well otherwise.

During the course of his illness he received five blood transfusions. Over a period of fifty-six days he was given 81.15 Gm. of sulfanilamide, with a daily average of 1.45 Gm. The sulfanilamide was continued over such a long period because of the slow progress made by the mastoid wound and not because of the meningitis.

Comment.—The patient recovered from a second attack of meningitis due to Str. haemolyticus.

This case is reported by permission of Dr. De Graaf Woodman.

CASE 11.—P. C., a white boy aged 17 years, was admitted to the Presbyterian Hospital with the history of a discharging left ear of two weeks' duration.

History.—The patient had had no infections of the ear. He had first been seen by a physician three days before admission. At that time his temperature had been 103.8 F., and he had had a severe headache. For the next three days his temperature had ranged between 100 and 103 F., and on the day of admission his temperature had risen to 104.5 F., and he had had definite signs of meningeal irritation.

Physical Examination.—Examination revealed a well nourished young man tossing about in bed and disoriented. The pupils reacted normally, and there was marked photophobia. The right ear was not diseased. The left external auditory canal was filled with a thick purulent discharge. The left drum was reddened and thick. There was no mastoid tenderness or sagging of the posterior wall of the canal. A slight amount of mucopurulent secretion was found in both nasal chambers. The neck showed marked rigidity. Reflexes were absent in the extremities, and Kernig's sign was positive.

A roentgen examination of the mastoids was reported by Dr. Ball as follows: "Stereoscopic films of the mastoids in the lateral and vertical views show small nonaerated cells on both sides in the processes but well aerated cells in the antral area and lower margin of the squamosa. There is a slight increase in the density of the right mastoid cells but no marked difference between the right and left."

Laboratory Findings.—The blood count was: hemoglobin, 95 per cent; white blood cells, 30,000; polymorphonuclears, 100 per cent.

The spinal fluid was under an initial pressure of 450 mm., turbid and colorless, containing no red blood cells and 20,000 white blood cells per cubic millimeter, with 70 per cent polymorphonuclears and 30 per cent mononuclears.

Gram stains of the spinal fluid smears revealed two short gram-positive chains of approximately 5 organisms.

Course.—On the basis of the above findings a left simple mastoidectomy under general anesthesia was immediately performed. The mastoid was found to be poorly pneumatized except in the periantral region. The cellular septums in the

periantral region were soft, and the cells contained granulation tissue. No free pus was seen. The dural and sinal plates were intact and appeared to be normal. The dural plate was entirely removed, and the dura was found to be under tension and had a bluish color. No peridural abscess was found. The patient was returned to the medical ward for treatment of the meningitis. That night he received 0.9 Gm. of sulfanilamide by clysis. Report of the cultures of the discharge from the middle ear and the spinal fluid on the following morning revealed a pure growth of Str. haemolyticus. The patient was given doses of 0.8 Gm. of sulfanilamide dissolved in 100 cc. of saline solution by clysis. On the second day after admission he received 6.8 Gm. and on the third day 4.7 Gm. The doses were slightly reduced for the next eight days, with an average of 3 Gm. daily. A lumbar puncture was performed daily for the first six days. The first three taps showed the fluid to be under pressure, and it contained Str. haemolyticus. Thereafter the spinal fluid did not contain the organisms, and the pressure gradually decreased to normal. On the eighth day after admission the patient's temperature was normal. During the next eight days, it rose gradually to 103.6 F. and remained elevated. The use of sulfanilamide was discontinued on the twenty-second day, and the temperature gradually returned to normal. The left middle ear was dry the day after operation, but the mastoid wound required a month for complete healing.

The patient was discharged on the thirty-eighth day after admission. He had received 76 Gm. of sulfanilamide over a period of twenty-two days. He has remained well.

Comment.—In a case of otitic meningitis due to Str. haemolyticus the patient recovered after a simple mastoidectomy was performed and sulfanilamide therapy was given.

This case is reported by permission of Dr. F. M. Hanger, who was in charge of the medical care.

OBSERVATIONS

There were many patients admitted to the hospital with acute otitis media who did not receive sulfanilamide and recovered. The question arises as to whether one is justified in giving an interpretation of results obtained by the use of the drug if patients will get well without it. Much clinical work remains to be done to show the difference between treated and untreated conditions. It is our feeling that the drug is of distinct value in all cases of acute otitis media due to Str. haemolyticus in which hospitalization is required and of probable value in those in which the condition is due to other organisms. Several patients with acute mastoiditis were admitted to the hospital and operated on without receiving the drug. All patients with cortical perforation were operated on. In our group, there were 4 patients with surgical mastoiditis, all of whom received sulfanilamide and recovered without surgical intervention. Livingston [1a] had 5 patients with surgical mastoiditis cured without operation. These observations do not prove anything, but they do allow one to lean toward conservatism in the treatment of acute mastoiditis.

Kopetzky [12] expressed the opinion that sulfanilamide will clear bodily fluids infected by streptococci, but it does not seem to kill streptococci located in an active osseous lesion. This was observed in the case of 1 of his patients, who had petrositis and meningitis.

Arnold [13] reported a case of streptococcic meningitis secondary to otitis media and mastoiditis, with peripheral facial paralysis. Sulfanilamide therapy was given before surgical intervention was resorted to. The patient recovered from the meningitis. and then a mastoidectomy was performed. Our patient (case 8, M. T.) had bacteremia secondary to otitis media and mastoiditis and recovered without operation. Patients who have meningitis or septicemia or both when first seen are not in the best operative condition. One wonders whether it would not be best to give the patient sulfanilamide for a few days before resorting to operation.

Lewy, in his article,[14] raised the question as to whether patients who have otogenic meningitis without surgical mastoiditis should be subjected to mastoidectomy.

It takes a large amount of clinical use of a drug to determine all its possibilities; therefore, it may be a long time before all questions regarding its place in otology are answered. One fact is certain: Progress has been made.

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CHRONIC SUPPURATIVE LESIONS OF THE PETROUS PYRAMID

REPORT OF SIX CASES WITH DIFFERENT PATHOLOGIC CHARACTERISTICS

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The good that has come from the prominence given in otologic literature to suppuration of the petrous pyramid has arisen not from the description of special surgical technics but from the fact that otologists have become more alert than formerly they were to the recognition of clinical syndromes and that they more clearly understand the pathologic processes that are associated with the condition.

The experience at the Mayo Clinic has been that each patient encountered has had to be regarded individually as far as diagnostic criteria and surgical intervention are concerned. Before the significance of symptoms and signs of lesions in the petrous pyramid was recognized, it is certain that some patients died because adequate surgical intervention was not instituted. The reported experiences of various observers have been extremely helpful in improving the clinical interpretation of symptoms and signs which previously had not been recognized as important.

As experience with the disease has increased, it has been more and more recognized that no limited and rigid symptom complex fulfils all requirements for the establishment of a diagnosis of petrositis. Further, exploratory operation on the basis of presumptive diagnosis has increased confidence by verifying the diagnosis, and, in addition, it certainly has saved lives that otherwise would have been lost.

Six cases of chronic suppuration of the petrous pyramid have been observed, in 5 of which a presumptive diagnosis was made after careful consideration and integration of symptoms and signs. The diagnosis was confirmed by an operation directed primarily to the petrous pyramid. If discharge from the ear, sepsis of low grade and deep retro-ocular pain had been insisted on as the cardinal symptoms and signs, the diagnosis would have been missed entirely. The 6 cases reviewed exem-

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plify different pathologic processes, ranging through caseated abscess and meningitis to thrombosis of the cavernous sinus, meningitis and rupture into the nasopharynx.

SUBACUTE PETROSITIS WITHOUT DISCHARGE FROM THE EAR

CASE 1.—A woman aged 39 presented herself at the clinic with a history that earache had developed on the right side five months previously. The pain was relieved in a few days by instillation of drops into the ear but recurred at frequent intervals throughout the next two months. A month before the patient's admission, the pain became more severe and more nearly continuous and was referred toward the occiput. At this time a roentgenogram of the mastoid process was made, but with negative results. The woman was found to have chronic sinusitis, and bilateral nasoantral windows were made. A few days after this operation the patient began to have pain deep in the right orbit and in the supraorbital and infraorbital regions on the right. She soon began to be awakened at night by severe pain in the right ear and mastoid region, and pain was referred to the right occipital region. These symptoms were still present at the time of her admission to the clinic. She stated that as far as she was aware the course of her illness had been entirely afebrile.

General physical examination and laboratory examination gave essentially negative results. Examination of her eyes revealed complete paralysis of the external rectus muscle on the right. The other extraocular muscles functioned normally. The ocular disks were of good color and had well defined margins. The ocular fields were normal. Neurologic examination gave negative results except for the findings enumerated. The spinal fluid was not examined.

The right tympanic membrane was bulging; the landmarks were not visible, and the whole drum was dull red. Tenderness was not elicited over the mastoid. A stapes fixation type of deafness was present on the right. Evidence of active paranasal sinusitis was not made out. A roentgenogram of the mastoid processes revealed diffuse cloudiness of the right mastoid process, with beginning absorption of the bony walls of the cells over the entire mastoid but especially marked over the lateral sinus. The anterior portion of the petrous pyramid seemed to be cellular.

A diagnosis of mastoiditis with anterior petrositis was made, and exploration of the right mastoid and petrosa was advised. At operation the mastoid process was found to be occupied by a cavity filled with pus and infected granulations. Because it was anticipated that disease was present on the anterior surface of the pyramid, radical mastoidectomy was performed, and the middle root of the zygoma was removed to the tegmen of the epitympanum to expose the cell tract shown by the roentgenogram to be medial to the zygomatic root. This tract was found to contain no pus, but the bone was hyperemic, and there was a little granulation tissue in the cells. Above the labyrinth, about midway between the cochlea and semicircular canals, red granular tissue was found, which when explored was seen to lead to the anterosuperior surface of the petrous pyramid. In this region a large epidural abscess was found. This was thoroughly drained, and the bone between the tract and the abscess was removed to facilitate drainage. Paralysis of the right abducens nerve had almost disappeared by the following day, and complete recovery from the paresis had taken place by the second postoperative day. Convalescence was without untoward incident, and the patient was dismissed from the hospital on the fourteenth day after operation. Four months after the operation the fistula leading to the anterior surface of the

petrous pyramid was still open, and there was slight purulent discharge. Subsequent observation of the patient disclosed that the wound was entirely healed and all the subjective symptoms had been entirely relieved.

CASEATED ABSCESS ON THE SUPERIOR SURFACE OF THE PETROUS PYRAMID

CASE 2.—A man aged 34 presented himself at the clinic for advice concerning paralysis of the right side of the face, of seven months' duration. He stated that the paralysis had started the morning after a ride in an open car and had become complete in about a week. He said that when he was 7 years of age he had a discharging right ear, but he could not recall details as to the severity of this illness. The ear had given him no further trouble.

On examination of the ears, nose and throat, the right tympanic membrane was found to be completely destroyed; the promontory was covered with a thick scar and stratified squamous epithelium. No secretion was seen in the middle ear or attic. Deafness of the right ear was noted.

General examination, including the serologic test for syphilis, gave negative results. Neurologic examination gave negative results except for the finding of a complete peripheral type of facial palsy on the right. A roentgenogram of the mastoids was reported to reveal complete sclerosis of the right mastoid, with no evidence of cholesteatoma. A diagnosis of Bell's palsy was made, and the patient was advised to return home, apply massage and electric stimulation to the muscles of the right side of the face and return for observation in a month.

On his return his condition was the same, and complete reactions of degeneration were observed on testing the right facial nerve with faradic stimulation. The man was seen again a month later, with his condition unchanged. Decompression of the right seventh cranial nerve in the fallopian canal was advised.

The right seventh nerve was readily exposed throughout its extent in the fallopian canal through an exposure like that for radical mastoidectomy, and change in the appearance of the nerve was not apparent. In the attic of the middle ear several small sequestrums were noticed. This observation seemed strange, because according to the history there had been no active disease for twenty-seven years. On exposure of the nerve above the promontory, as it turned below the anterior surface of the petrous pyramid, a peculiar white, cheesy material, appearing not unlike cholesteatoma, was encountered. The middle fossa was widely exposed and the temporal lobe elevated. The mass extended along the anterior surface to the apex and then back on the posterior surface to the internal auditory meatus. The facial canal had been eroded and the facial nerve pressed on by this mass in the region of the hiatus of the fallopian canal. It was concluded that the mass was the result of a parapetrous epidural abscess which had become sterile. Slight refrigeration, in the embarrassed state of the nerve, had been sufficient to produce the palsy. The postoperative course was uneventful, and the patient was dismissed from the hospital in a week. There has as yet been no evidence of returning function of the facial nerve.

The condition in the first case resembles "mucous otitis" of the masked type somewhat more closely than chronic petrositis, but it counterfeits almost exactly an acute stage of what could have been the course of events in the second case. In this second case it is believed that a similar abscess was rendered sterile and became desiccated by the defense mechanism of the body. It cannot be categorically denied that

the mass might have been a cholesteatoma originating from an epithelial outgrowth along the course of the fallopian canal and advancing from the epithelized middle ear. However, histologic examination of the cheesy mass removed at operation was said to show only desiccated and degenerated pus and no crystals of cholesterol. There can be no question that in the second case the cardinal symptoms of suppuration in the petrous pyramid were entirely lacking, as the diagnosis of the condition was made only at operation.

LATENT OSTEOMYELITIS WITH THROMBOSIS OF THE CAVERNOUS SINUS, MENINGITIS AND RUPTURE INTO THE NASOPHARYNX

CASE 3.—A boy 12 years of age was brought to the clinic in a semicomatose condition. The neck was retracted; the right eye appeared proptosed, and chemosis of the orbital conjunctiva was present.

A history was given that in the winter a year and a half previously the patient had had severe acute otitis media and mastoiditis, which had cleared up without surgical intervention. There was no further evidence of illness, and the boy was sent to a camp in northern Minnesota in the summer of 1935. Five days before his admission to the clinic he awakened in the morning with a right-sided headache and lancinating pain in the right side of the face; he was nauseated and vomited and had diarrhea and a temperature of 102 F. (38.9 C). His condition was unchanged the following day, but on the third day of illness the right tympanic membrane ruptured spontaneously, and profuse discharge began, with relief of the headache and a drop in the temperature. The next day the patient seemed somewhat better. The day following, the right side of the face became swollen, with protrusion of the right eye and edema of the eyelids. A physician was summoned, who found that the boy had marked photophobia. Also, there was tenderness over the tip of the mastoid process and in the neck, anterior to the right sternocleidomastoid muscle. Moreover, some rigidity of the neck was noted. Immediately the patient was taken to the nearest town, where spinal puncture was done. The fluid was said to have been under increased pressure and cloudy and to have contained 158 leukocytes to the high power microscopic field. The patient was brought by airplane to the Mayo Clinic.

On arrival, the boy lay with his eyes closed, but he could be aroused to answer questions. Rigidity of his neck was graded 1 on a basis of 1 to 4 in which 1 indicates a slight degree and 4 an extreme degree. Spinal fluid was cloudy, was under increased pressure and contained 1,000 leukocytes per cubic millimeter. Examination of smears of the spinal fluid did not reveal the presence of any micro-organisms, and there was no growth on culture in forty-eight hours. General and neurologic examination gave essentially negative results. There was a profuse purulent discharge in the right external auditory canal. The right tympanic membrane was red and thick. There was some tenderness on deep pressure over the right mastoid antrum. The eyes were prominent, but about equally so. The right lids were edematous, and the veins of both upper lids were dilated. There was some limitation of rotation of the right eye toward the right and downward. The fundi were normal; the margins of the disks were clear, and there was no venous engorgement. The ophthalmologist suspected that thrombosis of the cavernous sinus was present but thought that orbital cellulitis also could explain the findings.

By the next morning the lids of both eyes were edematous and injected, and ocular rotation was absent on both sides. The fundi were unchanged except for slight dilatation of the veins. The neck was rigid and retracted. A diagnosis of acute mastoiditis, with sympathetic meningitis and thrombosis of the cavernous sinus, was made. At the insistence of the parents and because smear and culture of the spinal fluid had been negative for organisms, exploration of the right mastoid process was done. The mastoid cells were hyperemic, and the pneumatic cells were of the diploic type. There were collections of pus in some of the cells. The temporal lobe was elevated, and the anterior surface of the petrous pyramid was explored, but no break was found. Postoperatively, the patient's condition seemed improved, and the spinal fluid contained only 300 leukocytes per cubic millimeter. The examination of cultures of this fluid disclosed an anaerobic streptococcus after forty-eight hours. The following morning there was a sudden discharge of purulent material from the nasopharynx, and in the afternoon the child suddenly became cyanotic and died in a few minutes.

Postmortem examination revealed thrombosis of the cavernous sinus, a diffuse, rather serous exudate over the base of the brain on the right side and chronic osteomyelitis of the inferior surface of the right petrous pyramid, with a fistulous tract leading down into the nasopharynx on the right. Culture of the pus from the osteomyelitic region yielded an anaerobic streptococcus which seemed identical with the one obtained on culture of the cerebrospinal fluid.

Although at the time this patient was under observation his condition seemed to us to be latent petrositis with later reactivation, it is impossible to deny that healing of the previous mastoiditis with fibrous tissue might have been in progress without the formation of new bone. These tracts of fibrous tissue, without much resistance to the propagation of infection, may have transported the bacteria rather rapidly from a region of recurrent otitis media to the dura and cranial sinuses. There may be a reasonable doubt that this was a case of true chronic petrositis without apparent otitis media. However, the finding of chronic osteomyelitis of the inferior surface of the petrous pyramid, together with the isolation of an anaerobic type of streptococcus both from the cerebrospinal fluid and from the chronic abscess found on examination of the body, tended to confirm the opinion that this process had been latent since the mastoiditis of a year and a half before. The three cardinal symptoms, sepsis of low grade, retro-ocular pain and postauricular discharge, certainly were absent throughout this period and also during the period of development of the meningitis and the thrombosis of the cavernous sinus. This case gave rise to the hypothesis that such a condition might occur and made the diagnosis easier and less open to doubt in subsequent cases.

CHRONIC PETROSITIS WITH NASOPHARYNGEAL FISTULA

CASE 4.—A woman aged 35 complained of extremely severe pain around the right ear and behind the right eye. Thirty years previously, material had drained from both ears. The condition of the left ear cleared up, but material continued to drain from the right ear, and for at least five years it had had a disagreeable

odor. There had been a constant, dull pain in the right ear for as long as the patient could remember. For the past ten years she had had an entirely different, severe, paroxysmal, lancinating pain, originating at a point behind the right mastoid process and extending forward to the right eye. These attacks had been present only when drainage from the right ear had stopped. She stated that when the pain was severe she was unable to see with the right eye. About a year before the patient came to the clinic she had an attack of scarlatina, during which she apparently had a high fever, with signs of meningeal irritation. Although the condition of the ear was suspected, she stated that her family had been told that her condition was hopeless and that operation was contraindicated. After this attack the discharge from the ear had been scanty and, when present, serosanguineous. The lancinating pains had been much more frequent and severe. Three months before the patient's admission to the Mayo Clinic, the lancinating pains had become almost continuous, and the patient had had a sensation of numbness and of pins and needles on the right side of the face. This paresthesia had been more pronounced the week before admission to the clinic. Also, the right upper lip had felt swollen; the lancinating pain, referred from behind the right mastoid process to the right eye, had reached its height, and the patient stated that she had been practically without sleep for a week. As far as she was aware, she had not had fever in the preceding year.

On admission to the hospital, general physical examination gave essentially negative results. Examination of the eyes did not reveal abnormalities; the ocular fundi and the fields, to which particular attention was given, were normal. The sense of smell and the sense of taste on the anterior two thirds of the tongue were diminished on the right side. Neurologic examination otherwise gave essentially negative results. The cerebrospinal fluid was normal in all respects. The right tympanic membrane was retracted, grade 3 plus. There was slight discharge. A high degree of conduction deafness was present on the right. There was a small fistula, from which a bead of pus drained into the right portion of nasopharynx, just posterolateral to the torus tubarius. Examination of the ear, nose and throat otherwise gave negative results. A roentgenogram disclosed the presence of complete sclerosis of the right mastoid process.

A diagnosis was made of chronic petrositis on the right, with probable involvement of the anterior and inferior surface of the apex, and exploration of the right petromastoid region was advised. At operation the mastoid cortex was seen to be sclerotic; the mastoid antrum was enlarged and was filled with granulation tissue. The upper knee of the sinus lay far forward, and on the outer surface was definite evidence of pachymeningitis. No cell tracts were found advancing around the posterior surface of the labyrinthine capsule. Radical operation was then done, and it was found that the ossicles were retracted forward and were firmly fixed just above the opening of the eustachian tube. When the ossicles were removed, it was found that they covered a fistula 0.5 cm. in diameter, filled with granulation tissue. The granulation tissue was removed, and an abscess cavity which seemed to involve the entire apex was entered. The fistula easily admitted a suction cannula, and the contents were aspirated through it. With a probe it was possible to palpate a soft region in the anterior aspect of the cavity. This was believed to correspond to the position of the carotid artery, while a soft region below was believed to represent the tissues of the nasopharyngeal vault. The patient was completely free of pain on waking from the anesthetic, made uneventful recovery and was dismissed from the hospital on the fifth day following operation.

The occurrence of long-continued attacks of severe, lancinating pain, evidence of dural irritation, which aroused fear of a fatal termination, together with a chronic discharge from the ear between attacks, should put the condition in this case in the category of chronic petrositis. The unusual occurrence of the fibrosed and retracted ossicles blocking the fistula to the apex of the pyramid, however, is one which might never be seen again. It seems that the nasopharyngeal fistula must have been the safety valve which prevented the explosion of meningitis. Although the cardinal symptom of pain behind the eye was present, low grade sepsis and profuse aural discharge were absent at the time of our examination.

CHRONIC CIRCUMSCRIBED PETROUS ABSCESS AND MENINGITIS WITHOUT APPARENT OTITIS MEDIA

CASE 5.—A girl aged 18 was first seen in January 1936. She complained of pain deep in the right side of her head, which was occasionally referred to the temple and upper teeth. Examination of the nose and throat gave essentially negative results. The tympanic membrane on the right showed scarring and thickening and a moderate degree of deafness due to fixation of the stapes was present in the right ear. The patient said that she had had otitis media with mastoiditis on the right side ten years previously. Although the discharge and tenderness over the mastoid had persisted for some time, the condition had finally resolved without mastoidectomy being necessary. This history was thought to explain satisfactorily the scarring of the right tympanic membrane and the conduction deafness. The otalgia persisted, however, and there was occasional projection of the pain to the occiput and the malar area on the right.

Six months after her first admission the patient began to complain of a sensation of "water" in her right ear, of earache with projection of the pain to the distribution of the right fifth nerve and of superficial tenderness over the right side of the face and mastoid. These symptoms disappeared spontaneously in about three days. Examination of the ears, nose and throat at this time again gave negative results except for some increase in the stapes fixation deafness on the right. About three weeks later these symptoms recurred, and there was in addition a sensation of giddiness. The results of examination at this time were the same as before, except that caloric examination of the function of the labyrinth revealed a slight hypersensitivity on the right. It was not thought that the ear had anything to do with the patient's symptoms. General examination at this time gave completely negative results; it included examination of the urine, determination of the leukocyte and the erythrocyte count and of the value for hemoglobin and serologic tests for syphilis. A roentgenogram revealed an impacted third molar in the right upper jaw. This was seized on as a probable explanation for the patient's symptoms, and the tooth was extracted. The symptoms again disappeared, but vertigo returned in about two weeks, markedly increased in severity. While the patient did not fall, on many occasions she had to support herself by holding onto the furniture. This continued for three weeks, after which, at 2 a. m., she was awakened by a severe bifrontal headache. This was intermittent at first but after three days became continuous. Following this, nausea and vomiting developed, and there was severe earache on the right. Until the onset of the meningeal symptoms, the patient had failed to show any elevation of temperature, and repeated leukocyte counts had been normal.

Neurologic examination revealed rigidity of the neck, grade 2 (on a basis of 1 to 4), and a positive Kernig sign. Spinal puncture was then performed; the spinal fluid was cloudy and was under a pressure of 26 cm. of water. It was found to contain 2.2 Gm. of protein per hundred cubic centimeters and 256 lymphocytes and 2,500 polymorphonuclear leukocytes. A Kline test of the spinal fluid for syphilis was negative. Smears of the spinal fluid revealed the presence of a gram-positive coccus, which could not be found on culture. A diagnosis of septic meningitis was made, and 10 cc. of meningococcus serum was given intrathecally. The next day continuous arachnoid drainage was instituted by means of a ureteral catheter inserted into the spinal arachnoid cavity.

Examination of the ears showed the same thick, rather white scarred membrane on the right that had been noted at the first examination. Tests of hearing revealed a completely nonfunctioning cochlea on the right, with normal hearing on the left. The caloric test for function of the semicircular canals revealed a completely nonfunctioning labyrinth on the right, with a normal response to a functional test on the left. Because it was suspected that a type III pneumococcus migh be present, the ear drum on the right was incised; a drop or two of clear serous fluid was released. A culture of this discharge was reported as negative. A roentgenogram of the petrous, temporal and mastoid regions of both sides was reported to reveal cloudiness in the right mastoid region, with beginning absorption of bone. This cloudiness was present throughout the right petrous pyramid. Examination of the eyes showed the function of the extraocular muscles to be normal and the ocular fundi to be negative.

The next morning there was paresis of the right side of the face, grade 1 to 2, and complete paralysis of the sixth cranial nerve on each side. In addition, there was partial paralysis of the right third cranial nerve, with ptosis, iridoplegia and cycloplegia.

In view of the history and findings, a diagnosis was made of septic meningitis secondary to inflammatory disease in the apex of the right petrous pyramid. Because of the complete nerve deafness and the nonfunctioning labyrinth on the right, a translabyrinthine approach to the right petrous apex was advised. At operation, the mastoid itself was found to be extremely sclerotic. There was no evidence of disease until the antrum was reached, when a slight amount of granulation tissue was found. The labyrinth was opened after the method of Neumann, and the canals were found to be filled with a blackish material. The petrous apex was then explored through the medial wall of the labyrinth, and an abscess, which appeared to be chronic and which contained thick white pus, was found. This abscess had uncovered the carotid artery for a distance of about 2 cm. The bone about the apex was softened and sequestrated in parts and was removed, an opening the full size of the petrous apex being accomplished. A rubber tube drain was placed down to the apex, and the upper portion of the mastoid wound was closed.

The intake of fluid postoperatively was kept to 4,000 cc. a day, any lack of fluid by the alimentary route being made up by the intravenous administration of 5 per cent dextrose in physiologic solution of sodium chloride. Two transfusions of 500 cc. each of citrated blood was given. Arachnoid drainage was stopped on the fifth day following operation. The paresis of the sixth cranial nerves and of the right third nerve had disappeared on the morning after operation. The facial palsy that followed operation was complete and showed no tendency to improve. Spinofacial anastomosis was performed six months later. The patient otherwise made an uneventful recovery and was dismissed from the hospital in six weeks.

Cultures of material from the abscess in the petrous apex did not grow readily; some growth of a streptococcus was obtained toward the bottom of tubes of brain broth, but the subculture was unsuccessful. This was thought by the bacteriologist to indicate an anaerobic organism of low virulence, such as might be encountered in an encapsulated abscess of long standing.

CHRONIC INTRACAPSULAR ABSCESS OF THE PETROUS BASE WITHOUT APPARENT OTITIS MEDIA

CASE 6.—A woman 47 years of age presented herself at the clinic with the history that in the afternoon four days previously she had suddenly noticed that she could not move the right side of the face. Within a few hours she began to have severe lancinating pains in the anterior portion of the right side of her face and forehead, with projection which was particularly marked along the zygoma and over the mastoid on the right. This pain was so severe that it required morphine for relief, and it had shown no tendency toward remission.

The patient said that ten years previously she had had a running ear on the right. This condition had recurred five years later. At that time there had been a discharge from this ear for about six weeks, and tenderness had been present over the mastoid. A year later, during a routine examination prior to tonsillectomy, many erythrocytes and albumin and casts had been found in the urine. The urine was then checked at monthly intervals; while it was occasionally clear, it usually showed a heavy cloud of albumin, casts and erythrocytes. Five months prior to admission, the patient began to have an occasional afternoon fever and general malaise. A leukocyte count showed 12,000 cells per cubic millimeter. About six weeks prior to admission, swelling of both parotid glands developed, and this swelling was still present at the time the patient was examined at the clinic. A cystoscopic and intravenous urographic examination made several weeks before her admission had been reported as negative; the excretion of phenolsulfonphthalein was 62 per cent in one hour.

General physical examination at the clinic gave negative results except for the urinary findings. A roentgenogram of the thorax showed no abnormality, and the serologic test for syphilis was negative. Examination of the blood showed the concentration of hemoglobin to be 12.78 Gm. per hundred cubic centimeters, and there were 4,360,000 erythrocytes and 4,500 leukocytes per cubic millimeter. The differential count was normal, and except for a slight shift to the left in the polymorphonuclear cells the blood smears showed nothing diagnostic. A culture of the blood was reported as showing no growth in forty-eight hours. An agglutination test was negative for Brucella abortus. The concentration of urea in the blood was 38 mg. per hundred cubic centimeters and that of sugar, 73 mg. The urea clearance test showed 55.6 cc. of blood cleared per minute, with a volume of 318 cc. of urine collected in one hour, the concentration of urea in the blood being 22 mg. per hundred cubic centimeters. The urine was acid; it had a specific gravity of 1.024 and contained albumin of grade 3, casts of grade 1 and erythrocytes and pus of grade 3 (on a basis of 1 to 4). The urologist expressed the opinion that the renal situation was not that of chronic glomerulonephritis but rather of a toxic condition secondary to renal irritation.

Neurologic examination revealed a peripheral type of palsy of the facial nerve on the right, slight anesthesia, grade 1, over the facial distribution of the fifth cranial nerve and an area of tenderness to percussion, grade 2 plus, over the right postauricular area. On examination of the ears, nose and throat, the right tympanic membrane was seen to be scarred and retracted (grade 3); acute

inflammation was not evident. A moderate degree of conduction deafness was present on the right. Caloric testing of the function of the labyrinth revealed a markedly hyperirritable labyrinth on the right. The nose, throat and nasopharynx were normal. Both parotid glands were enlarged (grade 1) and rather firm, and the superficial lymph nodes were palpable on both sides. There were tenderness to deep pressure (grade 3) over the right mastoid antrum and hyperesthesia to light pressure over the right mastoid and zygomaticotemporal region and over the supraorbital and infraorbital foramens on the right. A roentgenogram showed complete sclerosis of the right mastoid, with no evidence of involvement of the petrous pyramid.

The spinal fluid was clear and was under a pressure of 16 cm. of water; it contained 5 lymphocytes per cubic millimeter and 52.5 mg. of sugar and 714 mg. of chloride per hundred cubic centimeters. No organisms were found in the smears, and a culture of the spinal fluid was reported as showing no growth in forty-eight hours. The pupils and the function of the extraocular muscles were normal; the reaction of the pupils to light was graded minus 2. The ocular fundi showed mild edema around the margins of the nasal disk, with one fresh cotton wool patch in the left retina. There were a number of scars in the choroid of both eyes, which seemed to be the remnants of an old attack of choroiditis. It was the opinion of the ophthalmologist that these choroidal changes represented some form of long-standing toxemia.

After spinal puncture the lancinating pains in the right side of the face stopped almost immediately and did not return. Because of the history of aural trouble and of toxic nephritis dating from the last exacerbation of acute mastoiditis five years previously, together with the toxic choroiditis and evidence of sclerosis in the roentgenogram of the mastoid, it was suspected that a latent lesion might be present in the right temporal bone. The peripheral type of facial palsy and the evidence of irritation of the fifth and eighth cranial nerves led to the belief that a lesion was present in the petrous pyramid. The slight edema of the nerve heads in the ocular fundi and the presence of 5 lymphocytes in the spinal fluid, taken in conjunction with the fact that the lancinating pains in the face had stopped immediately after arachnoid drainage, made it certain that mild meningeal irritation, probably from the absorption of toxins, was present. The fact that the patient had no fever or leukocytosis during the five days of the examination suggested that the process was chronic. A diagnosis was made therefore of chronic encapsulated abscess in the right petromastoid, and exploration of the right temporal bone and contiguous dura was advised.

At operation the mastoid was found to be sclerosed completely, and the antrum was found to be small. In an attempt to expose the region overlying Trautman's triangle, a large cavity in the base of the pyramid was opened; this contained greenish opalescent fluid under some pressure. Microscopic examination of this fluid revealed a considerable quantity of cholesterol crystals. This cavity had outlined the posterior surface of the labyrinthine capsule down close to the internal auditory meatus; the dura, however, was not uncovered by the disease. This finding led to termination of the operation without decompression of the facial nerve or carrying out a more widespread exploration of the petrous pyramid. A Bondy modified radical operation was accordingly performed, and the postauricular wound was closed. Convalescence was uneventful. Movement became noticeable in the eyelids on the right and in the right angle of the mouth on the second day. The patient was dismissed from the hospital with the postauricular wound completely healed on the sixth day. Electrical reactions of the right side of the

face a week after the operation showed no degeneration, and a good prognosis for return of function in the facial muscles was given.

Examination of the eyes two weeks after operation was reported as showing no edema of the margins of the nasal disks. The choroiditis in the main seemed less active, although a few relatively recent patches were still present. The right eye could still not be closed fully, but the cornea could be covered. On the patient's dismissal from the clinic three weeks after the operation, the choroiditis was apparently inactive, but the urine still contained albumin, grade 3, and an occasional erythrocyte.

It seems probable that in cases 5 and 6 there was a chronic encapsulated abscess of the petrous pyramid, in the one apical and in the other basal. The gradual evolution of the symptoms over so long a period without any obvious initial illness seems to lend support to this hypothesis. The type of organism found in the spinal fluid and apical abscess in case 5 (an anaerobic organism of low virulence) suggests a long symbiotic type of existence in a closed focus. There seems to be no logical reason why a closed focus of this type cannot occur. Had exploratory operation not been performed on the basis of the presumptive diagnosis, the probabilities are that both patients would have succumbed to the disease.

SUMMARY AND CONCLUSIONS

Six cases have been presented in which various pathologic lesions of chronic petrositis were seen. Two were cases of encapsulated chronic petrositis without apparent otitis media. While it is not comforting to think of apparently healed mastoiditis or petrositis becoming active again after a period of five or ten years, nevertheless the conclusion that it can do so seems inescapable.

It is apparent that in certain cases in which there is an obscure clinical syndrome referable to the head the history of an ancient aural disease may assume a place of great importance in determining the lesion causing such a syndrome. Such cases as are here presented show the futility of attempting to fit clinical material into didactic or academic pigeonholes, because the cardinal symptoms and signs of petrositis were absent in whole or in part in each of the 6 cases. If the presence of the serious lesion in the petrous pyramid had not been suspected and exploratory operation had not been instituted before the appearance of complete symptoms and signs, the result might not have been so favorable.

The value of exploratory operations on the temporal bone when the condition is obscure and one feels strong probability of a serious disease has been demonstrated to our satisfaction. This group of cases demonstrates to us that it is necessary to approach the petrous pyramid without preconceived ideas regarding the surgical technic that will be adequate for the control of the disease encountered.

CYLINDROMA OF THE UPPER AIR PASSAGES

A CYLINDROMATOUS TYPE OF MIXED TUMOR

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The term cylindroma has been used by various authors to designate different tumors, which are most likely of diverse histogenesis. The name was first applied to an encapsulated orbital tumor, by Billroth [1] in 1856. He recognized in this neoplasm on gross examination two intertwining systems of cylinders, one composed of parenchymal cells and the other of hyaline or mucous stroma. The latter gave to the neoplasm a characteristic glassy appearance. Although Billroth regarded these as epithelial neoplasms, the cylindromatous appearance is due mostly to the stroma and only in slight part to the parenchyma. Although the term cylindroma is retained because of its descriptive as well as its historical value, it must be emphasized that it refers to a special type of mixed tumor in which the cylindromatous appearance predominates. The recognition of this entity has a deeper significance in that it implies a kinship to basal cell carcinoma. Because of this kinship some authors have in fact referred to cylindroma as basalioma.

Cylindromas occur most frequently in the salivary and lacrimal glands. They have also been described in the paranasal sinuses (Gutekunst [2] and Dembowski [3]), the trachea (Koschier [4]), the parenchyma of the lung (Heschl [5]) and the pharynx (Lang [6]). Various tumors, such as carcinoma and sarcoma, may have a cylindromatous appearance.

From the laryngologic service of Dr. Rudolph Kramer and the laboratories of the Mount Sinai Hospital.

1. Billroth, T.: Untersuchungen über die Entwicklung der Blutegefässe, Berlin, Georg Reimer, 1856.

2. Gutekunst, O.: Ein Fall von Cylindrom der Highmorshöhle, Arb. a. d. Geb. d. path. Anat. Inst. zu Tübingen **5**:1, 1904-1906.

3. Dembowski, T.: Onkologische Beiträge, Deutsche Ztschr. f. Chir. **32**:377, 1891.

4. Koschier, H.: Zur Kenntnis der Trachealtumoren, Wien. klin. Wchnschr. **9**:511, 1896.

5. Heschl, R.: Ueber ein Cylindrom der Lunge, Wien. med. Wchnschr. **27**: 385, 1877.

6. Lang, F. J., in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1929, vol. 5, pt. 2, p. 178.

The true cylindroma, however, seems to be a distinct entity, as originally described by Billroth.[7] Like a mixed tumor, it is well encapsulated, metastasizes only occasionally and rarely shows a tendency to carcinomatous transformation. However, when metastasis occurs the original histologic character of the tumor is retained in the metastasis.

HISTOGENESIS

In his original description of cylindroma, Billroth maintained that the tumor was of epithelial origin. In his later communication, however, he substituted the theory of an endothelial histogenesis. Early pathologists were divided in their acceptance of these two views.

Krompecher [8] showed the striking resemblance, both clinically and pathologically, of cylindroma to basal cell carcinoma of the skin. He referred to the former as hyaline solid basal cell carcinoma, hyaline adenobasal carcinoma and hyaline cystic carcinoma.

Considerable discussion has arisen as to the histogenesis of the framework of connective tissue which forms so large a component of the neoplasm. Some contend that the myxomatous, hyaline or mucinous contents of the cylinders are products of degeneration of the epithelial cells. They point to the small vacuoles which occur in the solid clusters of cells as the beginning of future tubular and cylindromatous transformation. From continued epithelial degeneration, large spaces result, which finally give the tumor its characteristic appearance. Others interpret the myxomatous substance within the cylinders as secretory products of the epithelial cells. The progressive hyalinization of this substance may lead to pressure atrophy of the surrounding epithelial cells. In such cases, the hyalinized stroma dominates the histologic picture.

Boemke [9] recently described 2 cases of cylindroma. He tried to explain the peculiar histologic character of the tumors as an abortive attempt at glandular formation. It is known that in the embryo glandular structure is first represented as a solid group of cells, which later becomes hollowed out by central degeneration. A duct is thus established between the acini and the surface. In cylindromas one similarly finds solid masses of proliferating epithelial cells. Boemke contended that in the latter instance the attempt at formation of a duct is imperfect in that the connective tissue grows rapidly into the lumen. With continued ingrowth of the stroma, which secondarily becomes hyalinized, the

7. Billroth, T.: Beobachtungen über die Geschwülste der Speicheldrüsen, Virchows Arch. f. path. Anat. **17**:357, 1859.

8. Krompecher, E.: Ueber die Beziehungen zwischen Epithel und Bindgewebe bei den Mischgeschwülsten der Haut und der Speicheldrüsen und über das Entstehen der Karzinosarkoma, Beitr. z. path. Anat. u. z. allg. Path. **44**:88, 1908.

9. Boemke, F.: Beitrag zur Histogenese und Malignität der Zylindrome, Centralbl. f. allg. Path. u. path. Anat. **64**:129, 1936.

glandular structure is not attained. An overgrowth of this hyalinized tissue results and causes pressure atrophy of the surrounding epithelial cells.

After study of our material, we feel that Krompecher's [10] theory of the origin of mixed tumors will also clarify the histogenesis of cylindroma. In our preparations several solid groups of cells strongly resembling the basal cells are to be found scattered throughout the

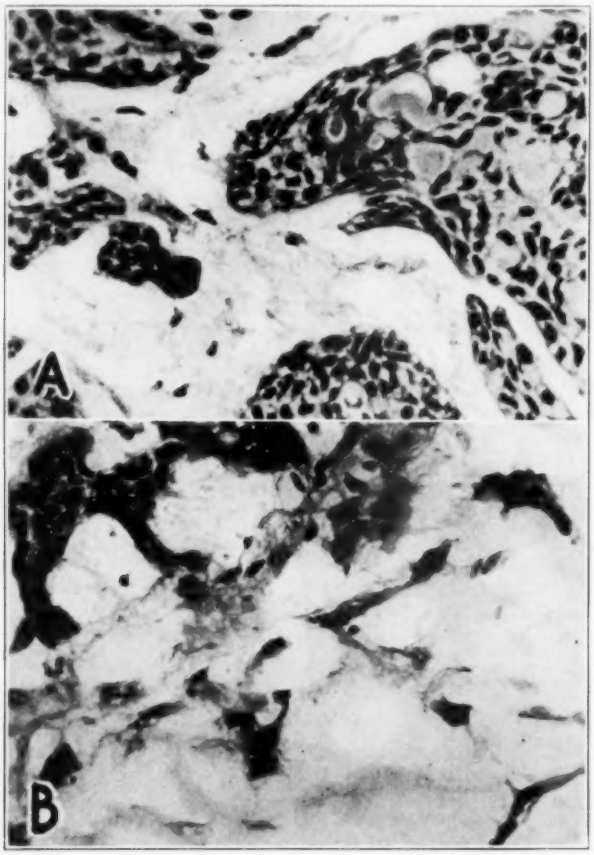

Fig. 1.—*A*, solid groups of cells resembling basal cells dominate the histologic picture. *B* (medium power), isolated epithelial cells separate from the main group above and assume a slightly elongated form.

section (fig. 1 *A*). These proliferating epithelial cells are numerous enough to dominate the histologic picture. Occasionally, one finds two or three isolated epithelial cells separating themselves from the main group and assuming a slightly elongated form (fig. 1 *B*). These cells

10. Krompecher, E.: Zur Histogenese und Morphologie der Mischgeschwülste der Haut sowie der Speichel und Schleimdrüsen, Beitr. z. path. Anat. u. z. allg. Path. **44**:51, 1908.

may or may not retain their connection with the solid mass of epithelial cells. Certain cells, thus isolated, become surrounded by a generous amount of myxomatous tissue, which is more abundant at a distance from the original mass of cells. Within this myxomatous tissue there are bizarre, star-shaped cells with elongated, tapering processes, which join those of neighboring cells in a reticular fashion (fig. 2 *A*). Such

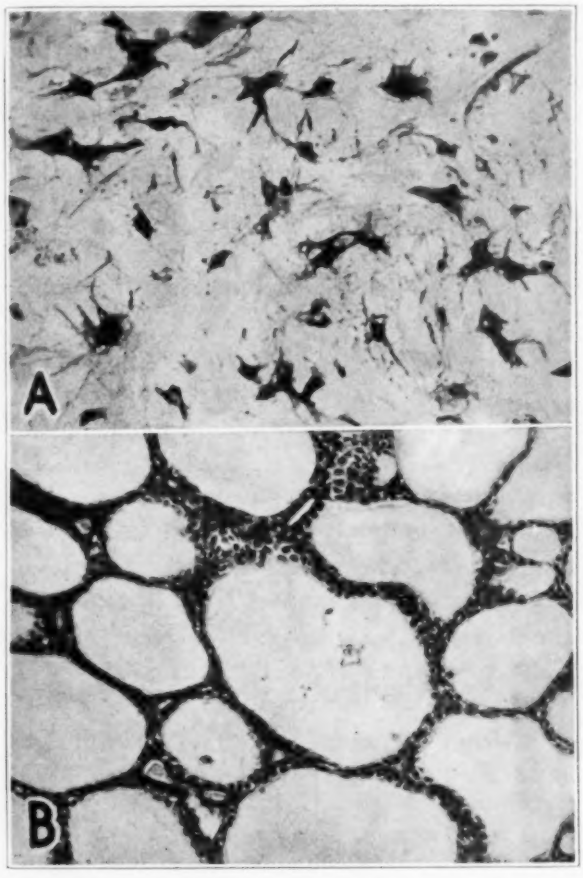

Fig. 2.—*A* (high power), bizarre, star-shaped cells, with elongated tapering processes, resembling mesenchymal cells are surrounded by a generous amount of myxomatous tissue. *B* (case 3), cylindroma of the trachea. The tumor resembles adenomatous tissue.

cells exhibit the same staining qualities as the basal epithelial cells. They strongly resemble the original mesenchymal cells of early embryonic life and seem to be a transition from the basal epithelial cells to the multipotent mesenchymal cells. Krompecher expressed the opinion that such transformations of epithelial cells to connective tissue cells may occur in the presence of a proliferating epithelium in a pliable stroma.

In cylindroma, it seems likely that some of the basal proliferating epithelial cells dedifferentiate into an immature cell having the potentialities of mesenchyma. This multipotent cell can now differentiate in another direction, with the production of various types of stroma. The myxomatous, hyaline and mucinous stroma found in cylindroma seems best explained in this way. The growth of the stroma found in cylindroma proceeds pari passu with the proliferation of the epithelial component, thus actively participating in the formation of the definitive tumor.

Distinctive features of the cylindroma are as follows:

1. The mucosa over the tumor is initially intact throughout, and the blood vessels are not very prominent on the surface.

2. The neoplasm, in most cases, is surrounded by a capsule which delineates the tumor from both mucosa and deeper structures. An ingrowth of septums from the capsule causes the tumor to be lobulated. In the trachea and bronchus, this produces a characteristic appearance.

3. On section, it has a glassy, grayish appearance. Microscopically, between the folds of epithelial strands, the spaces are filled with either mucous or hyaline substance.

4. The tumor is sessile and springs from a wide base involving the surrounding structures.

5. The neoplasm is slow growing, yet locally malignant. It is destructive both by pressure necrosis and by actual invasion.

6. There is a marked tendency to local recurrence, even after apparently thorough eradication of the tumor.

7. Distant metastasis is rare. When it occurs, the histologic character of the metastatic growth is identical with that of the primary tumor (Tommassi,[11] Ribbert,[12] Kornblith[13]).

8. Transition from cylindroma to carcinoma is indeed rare. Its occurrence, however, appears to verify the fundamental epithelial origin of the tumor. No case of sarcomatous transformation has been recorded.

Eigler[14] removed a hard, well encapsulated tumor from the base of the tongue, which proved histologically to be a cylindroma. After four local recurrences there finally occurred an invasion of the piriform

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11. Tommassi, C.: Ueber die Entstehungsweise des Friedreichschen Schlauchsarkoms, Virchows Arch. f. path. Anat. **31**:111, 1864.

12. Ribbert, H.: Ueber das Zylindrom, Deutsche med. Wchnschr. **33**:126, 1907.

13. Kornblith, A. B.: Zur Frage der Bösartigkeit der sogenannten Mischgewächse der Mundspeicheldrüsen, Virchows Arch. f. path. Anat. **286**:74, 1932.

14. Eigler, G.: Ueber Endotheliome, Peritheliome, und Cylindrom der oberen Luftwege, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **132**:208, 1932.

fossa and glandular metastases. The patient died of cachexia, and necropsy showed much atypism of the cellular tumor. There was comparatively little hyaline stroma.

Kornblith [13] regarded the proliferation of the epithelial strands in the connective tissue capsule as presumptive histologic evidence of the malignant transformation of the tumor.

Histologically the tumor resembles adenomatous tissue (fig. 2*B*). It is characterized by glossy, homogeneous hyaline or mucous cylinders with epithelial strands or spheres of cells resembling basal cells. Usually the spaces are surrounded by a rim of flattened cuboidal cells and resemble thyroid tissue. Individual cells are polyhedral and contain large nuclei rich in chromatin. Few vessels are to be found in the parenchyma of the tumor. The epithelial cells are of regular size and shape and stain with uniform intensity. Atypism and mitosis are not to be found.

Occasionally one finds solid masses of cells, among which small homogeneous collections of droplets are recognizable (fig. 3*A*). These may be the early stages of the glandular or tubular formations (fig. 3*B*). In other areas, columns of cells may be seen to spread between the hyaline cords and be lost therein (fig. 4*A*). Here one finds collections of cells which have no recognizable orderly arrangement. These cells may be round or stellate. Their cytoplasmic processes stain light pink with eosin. The nuclei are vesicular and partly chromatic and take a dark blue stain with hematoxylin. Such star-shaped cells, with their elongated, tapering processes, resemble mesenchymal cells.

Besides the contents in the cylinder, hyaline material is found dispersed throughout the tumor. In some areas, this hyaline material forms strands between the epithelial rows and by compressing them dominates the microscopic picture. Certain cells undergo pressure atrophy. Their nuclei lose their shape and appear pale in the surrounding structure.

The hyaline substance may be either a modified secretion or a result of the accumulation of the products of degeneration of the epithelium. It is possible also to have hyaline degeneration of an existing connective tissue. We have failed to throw additional light on the origin of the connective tissue by the use of selective stains.

The following differential and specific stains were employed in an attempt to distinguish qualitatively the various types of connective tissue stroma: Van Gieson, azan trichome, congo red, cresyl violet and Best's carmine.

With the Van Gieson stain the contents of the cylinders and tubes took an indefinite faint reddish color. The azan trichrome stain gave the myxomatous areas a faint blue or purplish blue hue. Congo red

and cresyl violet failed to show the presence of amyloid. Best's carmine indicated the nonmucinous character of the myxomatous stroma.

In the rare instances of metastasis the histologic character of the cylindroma is retained. Numerous reports have stressed the resemblance of the metastatic lesions to the primary tumor. Nussbaum,[15] Eigler [14] and Eidesheim [16] have recently reported metastasis to the pleura, lungs and vertebrae, with the retention of the original histologic character.

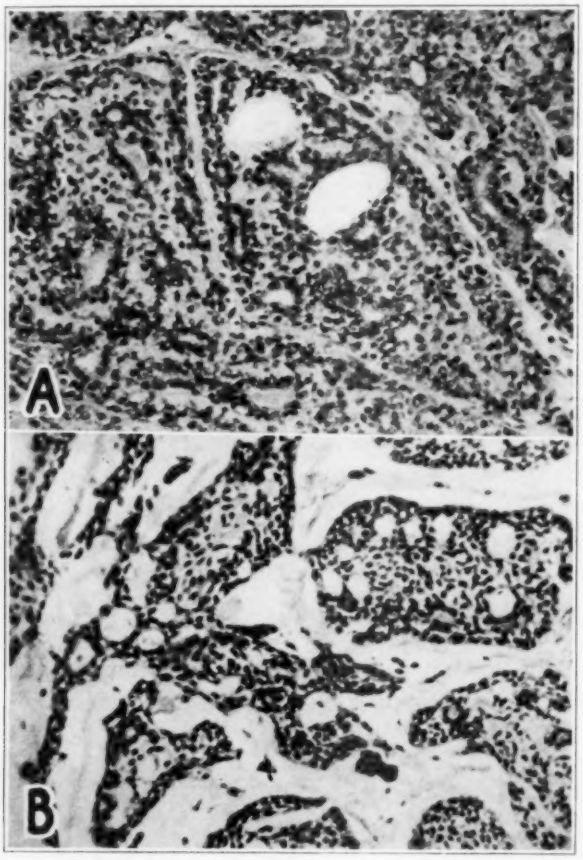

Fig. 3.—*A* (case 6), cylindroma of the bronchus; solid masses of cells, among which small homogeneous collections of droplets are recognizable. *B* (case 4), cylindroma of the bronchus. The myxomatous tissue in the circles may represent the early stages of tubular or glandular formations.

15. Nussbaum, R.: Ein Fall von Zylindrom des Warzenfortsatzes, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **125**:307, 1930.

16. Eidesheim, G.: Ein Beitrag zum Vorkommen primärer bösartiger Neubildungen in der Trachea (Cylindrom), Inaug. Dissert., Leipzig, E. Lehmann, 1909.

Metastasis was not observed in any of our series, but invasion of the capsule was frequently noted (fig. 4 *B*).

REPORT OF CASES

CASE 1.—R. B., a 50 year old male, was admitted to the Mount Sinai Hospital on Jan. 12, 1933, with a history of progressive impairment of hearing in the left ear of one month's duration, more marked during the last week. Some

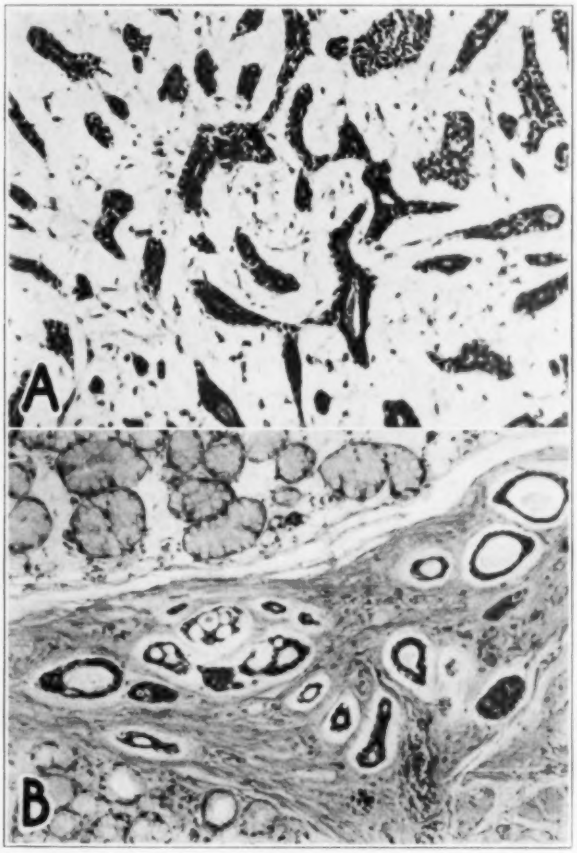

Fig. 4.—*A* (case 5), cylindroma of the bronchus; collections of cells showing no recognizable orderly arrangement; mixed tumor structure. *B* (case 2), cylindroma of the antrum; invasion of the capsule by a cylindromatous tumor, reported elsewhere as adenocarcinoma.

nocturnal pain had developed in the left ear. Examination revealed a man in generally good physical condition except for the local condition. The left drum was thick and congested and showed no landmarks. There was a slight thin discharge from an anterior perforation but no tenderness or sagging in the region of the mastoid. Left hemicranial headache developed, radiating to the temporo-occipital region. A simple mastoidectomy was performed and no evidence of

disease encountered. The culture was sterile. The mastoid wound healed in four weeks, but the violent temporo-occipital headache occurred intermittently. A granuloma protruding through the anterior perforation of the drum and filling two thirds of the fundus was now visible. Paralysis of the central part of the left side of the face, anesthesia of the left side of the face and contraction of the left pupil developed. Biopsy of the granuloma from the middle ear was reported to indicate squamous cell carcinoma. The patient received radiotherapy.

Five months later left palatal weakness and paralysis of abduction of the left vocal cord developed. There was some granular tissue, which bled readily, in the left fossa of Rosenmüller. A specimen of this tissue was then reported to be cylindroma. Radium emanation capsules were inserted in the left fossa, 97.3 millicuries for seven hours, giving a total of 681 millicurie hours. There was a marked recession of the lesion in the nasopharynx; yet another specimen was reported as cylindroma.

About one year after the mastoidectomy there was complete occlusion of the external auditory canal by the growth. The patient then had paralysis of the sixth and seventh cranial nerves, with involvement of the recurrent and hypoglossal nerves. He died of progressive cachexia.

The primary site of the tumor in this instance was probably in the nasopharynx, in or about the eustachian orifice. Growth of the tumor continued along the eustachian canal and into the middle ear. At this site it was recognized as tumor, and a biopsy proved it to be cylindroma. (A biopsy specimen from the nasopharynx was likewise reported to be cylindroma.) It may be that in some of the cases heretofore reported as instances of cylindroma of the mastoid bone the condition arose in this way. A recent communication by Nussbaum [17] cited a cylindroma of the mastoid bone, which apparently started in the posterior wall of the canal and invaded the entire mastoid bone to the extent of involving the facial nerve. As the hearing and the vestibular functions were normal and there was no evidence of the tumor in the nasopharynx, one must conclude that invasion of the mastoid bone in this particular instance was not by way of the eustachian canal. Cylindroma of the pharynx has been described by Lang.[6] Most examples of it arise around the base of the tongue or in the soft palate (Eigler [14]). In cases cited by Ribbert,[12] the primary tumor occurred in the submaxillary gland and invaded the pharynx secondarily.

Case 2.—B. K., a 23 year old woman, was first admitted to the laryngologic service of the Mount Sinai Hospital on Feb. 9, 1931. There was a history of nasal obstruction and pain in the right cheek, teeth and ear of two years' duration. Local treatment for the last two years had been of no avail. One year previously, the patient had consulted a dentist because of pain in the right upper jaw. A roentgenogram at that time revealed a rounded shadow in the right antrum situated above the first molar tooth. This was considered to be a cyst. Extraction of the tooth failed to give relief, and the floor of the antrum was explored by a horizontal incision above the margin of the gum.

17. Nussbaum, R.: Ungewöhnlicher Verlauf eines Falles von Zylindrom des Warzenfortsatzes, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **131**:13, 1932.

The patient had consulted us five months before admission to the hospital, because of spontaneous nasal hemorrhage, which lasted one week. A solid mass was noted in the right nostril, covered with dilated vessels. There was a firm nodular swelling of the right superior maxilla, with a scar on the alveolar surface. The right side of the hard palate felt nodular and was dislocated downward. The bone was absent in areas. There were enlarged deep cervical nodes on the right side. A biopsy specimen from the tissue in the right posterior naris was reported adenocarcinomatous by a leading pathologist.

High voltage roentgen therapy and radium pack were administered to the right side of the face. The molar prominence became less, but the mass extended into the left side of the nose and nasopharynx. The patient was then referred to the hospital.

On admission to the hospital, examination revealed a well nourished woman, not appearing ill. There were no palpable glands and no evidence of metastasis. Intranasal examination showed an invasion of the right nasal cavity by a growth extending through the middle and the inferior meatus. There were swelling and phlebectasia of the anterior wall of the right maxillary sinus and the hard palate. Roentgen examination showed cloudiness of the right antrum and frontal sinus, with a rounded mass 2 cm. in diameter on the floor of the antrum and an additional one extending into the nasal cavity posteriorly. The superior maxilla showed signs of absorption of bone. Sixteen needles, constituting 105 mg. of radium element, were inserted through the anterior wall of the antrum, the hard palate and the nasal cavity. These were allowed to remain twenty-four hours, so that the resultant dose was 2,500 milligram hours. Tissue removed for biopsy was now reported to be cylindroma. Considerable edema resulted from the application of radium but soon subsided.

The patient was readmitted on June 8, four months later, because of persistent swelling of the right maxillary region and hard palate with some drooping of the right corner of the mouth. There was a profuse mucopurulent discharge from both nostrils. With the patient under anesthesia induced by avertin with amylene hydrate, a Caldwell-Luc operation was performed on the right. The anterior wall of the superior maxilla showed rarefied bone, with an occasional defect. After removal of this, a dense capsule adherent to the molar region was encountered and freed from the bone. The capsule extended into the pterygomaxillary space posteriorly and along the anterior face of the orbital aspect and the floor of the antrum. The growth involved one third of the septum, extending into the left middle meatus. The entire neoplasm was removed by electrocoagulation. The bony floor of the right nostril was completely removed, and the free edge of the palatal mucosa was treated with diathermy. The postoperative course was complicated by a development of orbital cellulitis, which promptly subsided. A small necrotic area of palatal bone sloughed out.

The patient was readmitted in November 1934, three and one half years later. Examination now revealed a defect of the entire hard palate except for the posterior portion. The entire right wall of the nose to the superior turbinate was wanting and the interior of the antrum thus exposed. The middle half of the nasal septum was lacking. A smooth fine nodule about 1 cm. in diameter was present in the remaining portion of the hard palate. With the patient under anesthesia induced by avertin with amylene hydrate, excision of the residual hard and soft palate was performed, and the lateral wall of the nose was further coagulated. An obturator was prepared by the dental department. This closed off the roof of the mouth and permitted swallowing without nasal regurgitation.

Postoperatively there was considerable sequestration of bone, including part of the pterygoid plate. The wound healed completely.

The patient was readmitted on Oct. 24, 1935, because of extension of the growth on the posterior wall of the nasopharynx. Biopsy showed cylindroma again. She received treatment with a radium pack, the total dose being 875 milligram hours. The lesion became smaller, but the tumor persisted.

She was readmitted on Aug. 16, 1936, and received treatment with a radium pack to the extent of 290 mg. hours. There has been no recurrence of the tumor at the time of writing (June 1938). A roentgenogram of the chest showed no abnormality and there is no evidence of metastasis.

Cylindroma occurs more often in the antrums than in all the other accessory nasal sinuses combined. Beck and Guttman [18] collected 40 cases, in 23 of which the condition originated in the antrums. An isolated instance of primary cylindroma of the frontal sinus was reported by Dembowski.[3] Herzog [19] cited 1 case in which the growth occurred in the ethmoid sinus. Citelli [20] and Beck and Guttman [18] reported cylindroma which started in the sphenoid sinus. The original descriptions of cylindroma of the maxillary sinus were given by Krompecher,[21] Ribbert,[12] Ferreri,[22] and Gutekunst.[2] More recently Beck and Guttman [18] and Boemke [9] have contributed interesting accounts of cylindroma of the antrums.

The symptoms are those of any neoplastic disease of the maxillary sinuses, except that local glandular involvement and distal metastasis do not occur. The most effective therapy seems to be a combination of radical excision with diathermy, followed by protracted irradiation. The most rational operative approach is through the anterior wall (Caldwell-Luc) and includes, if necessary, removal of the floor of the antrum. A complete visualization of the contents and limits of the sinus is thereby obtained. Extension of the neoplasm to surrounding structures can be readily noted and eradicated. The resultant permanent palatal opening into the floor of the antrum minimizes the chances of a subsequent infection of the antrum. A distinct advantage is that it allows the cavity to be thoroughly investigated, and any recurrences may be detected and treated early. A properly constructed obturator prevents

18. Beck, J. C., and Guttman, M.: Basaloma or So-Called Cylindroma of the Air Passages, Ann. Otol., Rhin. & Laryng. **45**:618, 1936.

19. Herzog, G.: Zur Zylindromfrage, Centralbl. f. allg. Path. u. path. Anat. **31**:182, 1920.

20. Citelli, S.: Cylindrom des Sinus sphenoidalis, Arch. f. Laryng. u. Rhin. **15**:252, 1904.

21. Krompecher, E.: Der Basalzellenkrebs, Arch. f. Laryng. u. Rhin. **31**: 443, 1918.

22. Ferreri, G.: Contribution à l'étude clinique et anatomopathologique du cylindrome du maxillaire supérieur, Acta oto-laryng. **12**:411, 1928.

regurgitation into the nose, even in the presence of a large palatal defect.

We should like to stress again the value of irradiation, either by high voltage roentgen rays or by application of radium, in the treatment of these tumors. Eigler and Beck and Guttman reported on tumors of the antrum which responded to radiotherapy but subsequently recurred. In our own case, the radium pack was gratifying. The patient is still under observation for further recurrence.

CASE 3.—M. C., a 36 year old man, was admitted to the laryngologic service of the Mount Sinai Hospital on Nov. 26, 1934, with a history of increasing hoarseness for the past seven months. During the last five weeks he could not speak above a whisper. He noted a choking sensation and increasing dyspnea on the slightest exertion.

General examination gave negative results except for the local condition. The Wassermann and the Kahn test also were negative. Indirect laryngoscopic examination revealed in the subglottic area a smooth, red, rounded mass, covered with intact mucous membrane. The tumor arose from the right side and almost completely occupied the subglottic region. The vocal cords were uninvolved and freely movable. A tentative diagnosis of benign tumor was made. Roentgen examination of the neck before the operation showed a mass of soft tissue on the anterior wall of the trachea compressing the lumen below the region of the cricoid cartilage.

Tracheotomy was performed with the patient under local anesthesia, for the dual purpose of relieving the dyspnea and exploring the trachea. The neoplasm was found to be attached to the right lateral subglottic area, extending to the upper rings of the lateral tracheal walls below. The mass could not be enucleated in toto because of its extensive attachment. A specimen was removed, and a frozen section was reported as cylindroma. The major portion of the tumor was then removed with the aid of punch forceps. An adequate lumen was obtained, but it was considered that complete eradication of the neoplasm had not been performed. A tracheotomy tube was inserted.

A complete course of radiotherapy was administered by Dr. William Harris.

Four months later the patient was readmitted for decannulation. His larynx was uninvolved except for slight scarring of the anterior tracheal wall at the level of the tracheotomy opening. He has remained symptom free and shows no evidence of recurrence at the time of writing (June 18, 1938).

Epithelial tumors of the trachea are uncommon, and among these cylindroma is indeed a rarity. We have been able to find 7 authentic cases, to which we add our own.

In 1896, Koschier [4] described a nonulcerating tracheal neoplasm, which he termed carcinoma cylindromatosa. Heymann [23] reported a similar case of an extensive nonulcerating tracheal tumor in a 32 year

23. Heymann, R.: Beitrag zur Kenntnis des Epithels und der Drüsen des menschlichen Kehlkopfes im gesunden und im kranken Zustande, Virchows Arch. f. path. Anat. **118**:320, 1889.

old man. Since then, Henrici,[24] Eidesheim,[16] Segura [25] and Guttman [26] have cited similar instances. In the case reported by Simpson and Moore [27] as one of "primary adenocarcinoma of the trachea" the condition is probably more correctly classified as cylindroma. Their patient was a 32 year old woman with a localized, encapsulated tumor in the lower part of the trachea, without glandular involvement or metastasis. The histologic picture as published is that of cylindroma.

The striking feature of our case is the response of the tumor to radiotherapy. Total extirpation was not attempted because of the extensive involvement. The efficacy of protracted radiation therapy in this and other similar instances makes it a most valuable adjuvant in the treatment of cylindroma. Histologically, cylindroma is not an anaplastic growth, but a mature, well differentiated tumor of a type previously regarded as not amenable to radiation therapy. Members of the medical profession must modify their views so as to regard these mature neoplasms as occasionally radiosensitive.

Case 4.—H. S., a 33 year old man, was admitted to the laryngologic service of the Mount Sinai Hospital on Feb. 25, 1928, with a history of cough, chilliness and fever, with pain in the right side of the chest, aggravated by breathing. He had had several attacks of hemoptysis and lost 5 pounds (2.3 Kg.). There were signs of atelectasis of the lower lobe of the right lung. A roentgenogram showed a dense shadow occupying three fourths of the right side of the chest. The volume of the right side of the chest was diminished, with marked displacement of the heart and mediastinum to the right. Aspiration of the lung yielded no tumor cells. Bronchoscopic examination revealed a bilobed, rounded mass covered with normal mucous membrane and dilated vessels just below the upper lobe of the right lung. There was a good deal of secretion below this. The right bronchus was completely occluded by the tumor. Biopsy was reported as indicating adenocarcinoma. Ten radium seeds were inserted; one week later 6 were removed. The following week the remaining 4 seeds were removed. Breath sounds began to come through, and crepitant rales appeared. The patient died two months later of pulmonary hemorrhage. Reexamination of slides at a later date showed that the tumor was not an adenocarcinoma but a cylindroma.

Case 5.—H. P., a 53 year old woman, was admitted to the Mount Sinai Hospital on June 3, 1935. She gave a history of recurrent hemoptysis for the past two years. The right side of the chest was flat; breath sounds did not come through, and the mediastinum was drawn to the right.

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24. Henrici, I.: Ein Beitrag zur Kenntnis der Trachealtumoren, Arch. f. Laryng. u. Rhin. **17**:282, 1905.

25. Segura, E. V.: Un cas de cylindrome tracheal operation par voie externe, Ann. d. mal. de l'oreille, du larynx **39**:162, 1913.

26. Guttman, M. R.: Primary Adenocystic Carcinoma or Cylindroma of the Trachea, Ann. Otol., Rhin. & Laryng. **45**:894, 1936.

27. Simpson, W. L., and Moore, R. M.: Primary Colloid Adenosarcoma of the Trachea, Ann. Otol., Rhin. & Laryng. **43**:1135, 1934.

At bronchoscopic examination on June 7, a lobulated, polypoid-looking mass, which did not bleed readily, was found obstructing the right main bronchus at the carina. It was attached to the posterior wall of the bronchus. The major portion of the tumor was removed with a punch forceps. The specimen was reported as cylindromatous (fig. 4 *A*).

The patient was given a bronchoscopic treatment on June 16. The remaining part of the tumor and the tissue were removed, and the base of the tumor was coagulated with diathermy. She became symptom free.

At bronchoscopic examination on April 4, 1936, some thickening was observed on the posterior wall of the right main bronchus; otherwise the condition was normal.

The patient has remained symptom free ever since. Recent bronchoscopic examination, on March 10, 1938, revealed some nodular thickening of the right main bronchus at the original site of the tumor. Biopsy was again reported as indicating cylindroma. The histologic picture is identical with that of the original specimen. In spite of local recurrence of the growth, there are no symptoms or signs referable to the tumor.

CASE 6.—T. R., a 36 year old man, was admitted to the laryngologic service of the Mount Sinai Hospital on Feb. 24, 1936. There was a history of three attacks of pneumonia of the upper lobe of the left lung within the past two years. For the last five weeks he had complained of a dry cough and pain in the left side of the chest. Roentgen examination of the chest showed a homogeneous shadow in the left pulmonary field between the seventh and the eighth rib posteriorly. In addition, the heart and trachea were drawn to the left; the diaphragm was elevated on the same side, and narrowing of the intercostal spaces was noted.

Bronchoscopic examination revealed a polypoid tumor at the orifice of the bronchus of the upper lobe of the left lung. The tumor partly protruded into the tracheal lumen on cough. The mass appeared lobulated and was covered with a smooth, grayish white mucosa. It did not bleed readily on probing. The major portion of the tumor, which occluded the upper lobe of the left lung, was removed. A biopsy was reported as indicating cylindroma.

The patient was given two more bronchoscopic examinations at weekly intervals. The remaining tumor growth was removed, and some thick creamy pus was aspirated from the left anterior descending branch of the upper lobe of the left lung.

Bronchoscopic examination two months later showed some thickening at the spur of the upper lobe of the left lung.

The patient was readmitted on Feb. 24, 1938, for a check-up. He was completely symptom free. At bronchoscopic examination no abnormalities were noted except some slight thickening of the spur of the anterior descending branch. A biopsy showed no recurrence of the growth.

COMMENT

No other cases of cylindroma of the bronchus have been reported in the literature.

The condition should be suspected whenever a smooth, lobulated tumor covered with normal mucosa is encountered bronchoscopically. The tumor grossly resembles benign adenoma, from which it can be differentiated only microscopically. It is most important not to confuse

cylindroma with bronchial carcinoma, as the therapy and ultimate prognosis are decidedly different. Whereas the latter offers a grave outlook regardless of the therapy employed, the former can be removed bronchoscopically and the patient rendered symptom free. The responsibility for detecting cylindroma rests with both the endoscopist and the pathologist. Early recognition of the true nature of the tumor may prevent an untimely fatal outcome because of procrastination.

In case 4, the neoplasm was not removed, because of the mistaken belief that we were dealing with adenocarcinoma. The patient received radium implantation and succumbed to a fatal hemorrhage. In the subsequent 2 instances the true nature of the neoplasm was recognized and removal of the tumor performed. The patients have been symptom free, although 1 still has some residual cylindroma.

It is possible that some cases of cylindroma have been reported heretofore as adenocarcinoma. As the outlook is so different, extreme care should be exercised not to confuse the two conditions.

The clinical symptoms of bronchial obstruction, viz., atelectasis, recurrent pneumonia, hemoptysis and bronchiectasis, subsided in our 2 cases after the tumor was removed and the patency of the bronchial lumen restored. Repeated bronchoscopic examinations should be performed in order to eradicate all the neoplastic tissue, and the base may then be treated with diathermy if necessary. Subsequent endoscopic examination will be necessary to watch for and treat recurrences.

SUMMARY

The term cylindroma refers to a special type of mixed tumor, which has a kinship to basal cell carcinoma. It occurs most frequently in the salivary glands but has been described in the paranasal sinuses, pharynx, trachea and lungs. The tumor usually appears as an encapsulated, sessile neoplasm covered by intact mucosa. Although slow growing, it is locally malignant and shows a marked tendency to recurrence. Distant metastasis and transition to carcinoma are rare.

The clinical history, pathologic picture and therapy in 6 cases of cylindroma of the upper air passages are presented. In 2 instances, the initial pathologic report elsewhere was that the growth was an adenocarcinoma. In a third instance, a preliminary diagnosis, based on a biopsy, was immature squamous cell carcinoma, but after further study, of a more adequate specimen, the diagnosis was cylindroma. Differentiation from adenocarcinoma is essential to proper therapy and to more accurate prognosis. Once the condition is recognized as cylindroma, local excision with diathermy followed by radiotherapy offers the best prognosis.

121 East Sixtieth Street.

Case Reports

PNEUMOCOCCIC MENINGITIS WITH RECOVERY

Combined Use of Serum and Sulfanilamide

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Recovery from pneumococcic meningitis is sufficiently rare and unusual to warrant the reporting of a single case. That sulfanilamide is the sine qua non of antistreptococcic therapy is undisputed; its use for pneumococcic infection is not yet fully established.

Meakins,[1] Musser,[2] Cecil[3] and others[4] have expressed themselves as one in describing the disease as highly virulent and invariably fatal. Tripoli,[5] out of his ten years' experience at the Charity Hospital in New Orleans, reported 1 recovery in 111 cases of pneumococcic meningitis. His patients were treated with pneumococcic monovalent and polyvalent serum and with a pneumococcus vaccine. The 1 patient to recover was treated with polyvalent antimeningococcus serum by combined lumbar and cisternal puncture!

Neal and Appelbaum[6] reported 14 cases of pneumococcic meningitis, with 3 recoveries. None of the patients who recovered received serum.

Rosenthal[7] has shown that sulfanilamide is bacteriostatic and bactericidal for pneumococci in vitro, while it does not inhibit the growth of the hemolytic streptococcus. Colebrook, Buttle and O'Meara[8] and

1. Meakins, J. C.: The Practice of Medicine, St. Louis, C. V. Mosby Company, 1936, p. 981.

2. Musser, J.: Internal Medicine, Philadelphia, Lea & Febiger, 1936, p. 136.

3. Cecil, R. L.: A Text Book of Medicine, Philadelphia, W. B. Saunders Company, 1937, p. 145.

4. Griffith, J. P. C., and Mitchell, A. G.: Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1937, p. 900. Boyd, W.: Text Book of Pathology, Philadelphia, Lea & Febiger, 1938, p. 910. Grinker, R. R.: Neurology, Springfield, Ill., Charles C. Thomas, Publisher, 1937, p. 659. Holt, L. E., Jr., and McIntosh, R.: Diseases of Infancy and Childhood, New York, D. Appleton-Century Company, Inc., 1934, p. 1019.

5. Tripoli, C. J.: Bacterial Meningitis: A Comparative Study of Various Therapeutic Measures, J. A. M. A. **106**:171 (Jan. 18) 1936.

6. Neal, J. B., and Appelbaum, E.: Experience with Sulphanilamide in Meningitis, Am. J. M. Sc. **195**:175 (Feb.) 1938.

7. Rosenthal, S. M.: Studies in Chemotherapy: Effect of p-Aminobenzenesulphonamide on Pneumococci in Vitro, Pub. Health Rep. **52**:192 (Feb. 12) 1937.

8. Colebrook, L.; Buttle, G. A. H., and O'Meara, R. A. Q.: Mode of Action of Para-Aminobenzenesulfonamide and Prontosil in Hemolytic Streptococcic Infections, Lancet **2**:1323 (Dec. 5) 1936.

Long and Bliss,[9] however, found that sulfanilamide is bacteriostatic in vitro to streptococci in small numbers and expressed agreement with the findings of Fuller [10] and Rosenthal [7] that neither the original prontosil [11] nor prontosil soluble [12] has a bacteriostatic or bactericidal action in vitro. Independently, these workers [13] and Fuller [10] concluded that either of the prontosils must be reduced in the body to become active and that activation is brought about by infection with a hemolytic streptococcus. Fuller,[10] stated the belief that the action of the prontosils is due to the sulfanilamide derived from them by reduction in the body. Gross and Cooper [14] succeeded in prolonging and saving the lives of rats experimentally infected with the type III pneumococcus by oral feedings of sulfanilamide. Rosenthal,[15] too, could save infected mice with sulfanilamide, but he found that the prontosils had no curative effect.

Branham and Rosenthal [16] found that for experimental pneumococcic infections in mice a combination of serum and sulfanilamide yielded better results than the use of either alone. The results of Buttle and his co-workers [17] were not as encouraging, nor did Cooper and Gross [18] find a combination of serum and sulfanilamide more effective than the use of either alone.

After oral administration, sulfanilamide is absorbed from the gastrointestinal tract in about four hours. The drug passes rapidly from the

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9. Long, P. H., and Bliss, E. A.: Para-Amino-Benzene-Sulfonamide and Its Derivatives: Experimental and Clinical Observations on Their Use in the Treatment of Beta-Hemolytic Streptococcic Infection; Preliminary Report, J. A. M. A. **108**:32 (Jan. 2) 1937.

10. Fuller, A. T.: Is Para-Aminobenzenesulphonamide the Active Agent in Prontosil Therapy? Lancet **1**:194 (Jan. 23) 1937.

11. The hydrochloride of 4-sulfamido-2′,4′-diaminoazobenzene.

12. The disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonic acid.

13. Colebrook, Buttle and O'Meara.[8] Long and Bliss.[9]

14. Gross, P., and Cooper, F. B.: Efficacy of Para-Aminobenzenesulfonamide in Experimental Type III Pneumococcal Pneumonia in Rats, Proc. Soc. Exper. Biol. & Med. **36**:225 (June) 1937.

15. Rosenthal, S. M.: Studies in Chemotherapy: Chemotherapy of Experimental Pneumococcus Infections, Pub. Health Rep. **52**:48 (Jan. 8) 1937.

16. Branham, S. E., and Rosenthal, S. M.: Studies in Chemotherapy: Sulphanilamide, Serum and Combined Drug and Serum Therapy in Experimental Meningococcus and Pneumococcus Infections in Mice, Pub. Health Rep. **52**:685 (May 28) 1937.

17. Buttle, G. H.; Parish, H. J.; McLeod, M., and Stephenson, D.: Chemotherapy of Typhoid and Some Other Non-Streptococcus Infections in Mice, Lancet **1**:681 (March 20) 1937.

18. Cooper, F. B., and Gross, P.: Sulfanilamide, Antipneumococcus Serum and Vitamin C Therapy in Type II Pneumococcal Pneumonia in Rats, Proc. Soc. Exper. Biol. & Med. **36**:5 (June) 1937.

blood to the tissues and appears in the spinal fluid in almost as high a concentration as in the blood.[10]

There is much confusion as regards the mode of action of sulfanilamide. Colebrook [8] expressed the opinion that treatment with sulfanilamide increases the bactericidal power of the blood serum. Long and Bliss [9] stated that "phagocytosis plays a paramount role." Bigler, Clifton and Werner [20] decided that the action of sulfanilamide was independent of the leukocytes, while Osgood [21] stated that "the major action of sulfanilamide appears to be on the production of toxins or aggressins."

REPORT OF A CASE

S. D., a well nourished and well developed 20 year old white woman was admitted to the Shore Road Hospital on April 19, 1938, in a semicomatose state. Her temperature was 104 F., her pulse rate 110 and her respiratory rate 22. At the age of 5 years she had had an anterior fracture of the skull, over the right frontal sinus, at which time a piece of comminuted bone was removed.

On April 14, the patient complained of a cold and running nose and treated herself with the usual home remedies. On April 17, she was seen at home, complaining of pain over the right maxillary antrum, a purulent nasal discharge and a postnasal drip. The next day she was seen at the office; the pain was lessened, and she felt improved. Late the next night, April 19, she became suddenly worse, vomited and did not recognize her relatives. She was seen shortly after. Her temperature was 104 F. and her pulse rate 120, and she complained of pain of the right frontal sinus. There was nuchal rigidity, and a Kernig sign was elicited; the patient was turned away from the light. A diagnosis of meningitis secondary to frontal sinusitis was made, and the patient was hospitalized at 10:30 that night, about two hours after the onset of meningeal signs.

On admission a spinal tap was done. The fluid was cloudy and under pressure and contained 14,000 cells with 98 per cent polymorphonuclears. A smear revealed a gram-positive, encapsulated extracellular diplococcus, morphologically resembling the pneumococcus. Cultures were made and a specimen sent to Dr. Neal, who after thirty-six hours hours reported a type VII pneumococcus. The urine was normal. A blood count revealed red blood cells, 3,800,000, with 69 per cent hemoglobin, and white blood cells, 17,000, with 95 per cent polymorphonuclears.

A consultant, Dr. Louis Blumenfeld, saw the patient at midnight. His examination and impression were as follows: "The patient appears critically ill. The general symptoms, stupor, rigidity of the neck, high temperature and positive Kernig sign, together with marked local tenderness over the right frontal sinus and a purulent discharge from the right nasal chamber, point to acute frontal empyema. The right frontal sinus and the right antrum do not transilluminate. There is a history of fracture of the skull in the right frontal area fifteen years ago. This injury necessitated surgical intervention, as is evidenced by a surgical scar. The findings and history lead one to the diagnosis of acute meningitis secondary to frontal empyema, with the point of entry of the organisms into the meninges probably the site of the old fracture."

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19. Marshall, E. K., Jr.; Emerson, K., Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide: Absorption and Excretion; Method of Determination in Urine and Blood, J. A. M. A. **108**:953 (March 20) 1937. Proom, H., and Buttle, G. A.: Para-Aminobenzenesulphonamide in Bacterial Meningitis, Lancet **1**:661 (March 13) 1937.

(Footnotes continued on next page)

An external operation for frontal empyema was advised. Prontosil solution,[22] 15 cc. every four hours, was prescribed, and morphine sulfate for restlessness.

The next morning, April 20, a spinal tap was done. The fluid was cloudy and under pressure. There were 15,000 cells. A roentgenogram of the skull revealed ". . . bilateral frontal sinusitis, more marked on the right side, which is probably purulent, bilateral ethmoid sinusitis, with possible early involvement of bone on the right side, and empyema of the right maxillary sinus. Directly over the frontal sinus and close to the midline on the right side is an area of rarefaction in the frontal bone, the nature of which is not evident from the films. It may be due to old operative work as the history suggests."

The patient was vomiting and irrational, her temperature being 104 F. and her pulse rate 110. Fifty cubic centimeters of 50 per cent dextrose was given intravenously and the patient morphinized and taken to the operating room.

The region of the right frontal sinus was anesthetized with 0.5 per cent procaine hydrochloride. The area of the right frontal sinus was uncovered with an L-shaped incision. The sinus was opened with a small chisel and the anterior wall removed. The cavity was filled with a creamy pus, which was aspirated by suction. A specimen was taken for culture. At the upper right angle of the frontal sinus a granuloma was found, which was adherent to the dura. There was no bony covering; it had evidently been removed at the previous operation for fracture of the skull. The inner plate of the sinus was removed and an inflamed dura revealed. The bone around the granuloma was removed. The dura appeared to be under tension and protruded somewhat into the sinus. Under antiseptic precautions a fine needle was introduced beneath the dura, but no pus or fluid was obtained. The dura and the cavity of the sinus were painted with a dilute iodine solution. The cavity was flushed with sulfanilamide, 0.8 per cent solution, and loosely packed with iodoform gauze, which was saturated with the solution. The cutaneous flap was replaced without sutures and a dressing applied. A continuous wet dressing of sulfanilamide, 0.8 per cent solution, to the operative wound was ordered.

The specimen of pus taken for culture was reported after forty-eight hours as a gram-positive, encapsulated diplococcus, bile soluble—a pneumococcus.

After the operation the patient's temperature fell to 100.8 F. She was irritable and complained of pain in the head and neck. Nuchal rigidity was present, and she was still vomiting. A clysis of 1,000 cc. of saline solution was given. Codeine and morphine sulfate were necessary to combat restlessness. The use of the wet dressing of the sulfanilamide solution was continued.

On April 21 her temperature rose to 104 F. A spinal tap was done and 30 cc. of cloudy fluid removed. There were 8,600 cells. The fluid was cultured at the hospital laboratory and a specimen sent to Dr. Neal. After forty-eight hours both were reported as containing a type VII pneumococcus. The reaction for albumin was 3 plus and for globulin 3 plus; there was no sugar. Twenty cubic centimeters

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20. Bigler, J. A.; Clifton, W. M., and Werner, M.: The Leukocyte Response to Sulphanilamide Therapy, J. A. M. A. **110**:343 (Jan. 29) 1938.

21. Osgood, E. E., and Brownlee, I. E.: Culture of Human Marrow: Studies on the Mode of Action of Sulfanilamide, J. A. M. A. **110**:349 (Jan. 29) 1938; The Mode of Action of Sulphanilamide, ibid. **110**:1770 (May 21) 1938.

22. The prontosil used in this work was the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonic acid, which was administered in the form either of a 2.5 per cent solution or of a powder, supplied in 5 grain (0.32 Gm.) capsules by the manufacturer.

of sulfanilamide, 0.8 per cent solution, was introduced intraspinally by gravity. There was no rise in temperature. The patient was still vomiting; nuchal rigidity was present, and she complained bitterly of pains in the head and neck. She was irrational and delirious at times. Five hundred cubic centimeters of a solution of dextrose was given intravenously. (The dosage of sulfanilamide and prontosil [22] is described in the table.)

On April 22 the patient's condition was essentially unchanged. She was irrational at times and still vomiting, though less frequently. A spinal tap was done and 15 cc. of cloudy fluid removed. The cell count was 4,600. The dressing was changed. There was some discharge.

On April 23 vomiting was less frequent, but she was still irrational at times. A spinal tap was done and 20 cc. of cloudy fluid removed. The cell count was 1,750. A blood culture was taken and after seventy-two hours reported as negative. A prontosil concentration test was negative! Five hundred cubic centimeters of 5 per cent dextrose was given intravenously. The application of sulfanilamide in wet dressings was continued.

On April 24 the patient's temperature was 102 F. A spinal tap was done and 15 cc. of cloudy fluid removed. The cell count was 1,900. Vomiting had ceased. The patient was still irrational at times and was complaining of photophobia and diplopia. The dressing was changed; there was a slight discharge.

The next day, April 25, her temperature rose to 105 F. A spinal tap was done and 20 cc. of cloudy fluid removed. A cell count revealed 4,700 cells. Five cubic centimeters of prontosil solution,[22] 2.5 per cent, and 10 cc. of saline solution were introduced into the spinal canal by gravity; 40,000 units of combined type V and VII pneumococcus serum (horse) was given intramuscularly. A specimen of the spinal fluid was sent to Dr. Neal's laboratory for culture, and after forty-eight hours it was reported as negative. The reaction for albumin was 2 plus, that for globulin, 2 plus, and that for sugar, 2 plus. The patient was irrational, complaining of headache and nuchal rigidity. The application of wet dressings with sulfanilamide to the operative area was continued. That evening a spinal tap was again done. Thirty cubic centimeters of orange fluid was removed. The cell count was 2,500. Ten cubic centimeters of prontosil solution [22] 2.5 per cent and 40,000 units of the combined serum were introduced intraspinally by gravity. The patient was disorientated and irritable. After the intraspinal injection of the serum and the prontosil [22] solution, her temperature rose to 106 F.

On April 26 a spinal tap was done, and 12 cc. of an orange fluid was removed. The cell count was 2,600. Forty thousand units of combined serum was given intramuscularly. The patient was irrational at times. Five hundred cubic centimeters of 5 per cent dextrose was given intravenously. The temperature that evening fell to 102 F. She still complained of diplopia. The dressing was changed; there was a slight discharge.

The next day, April 27, definite improvement was noted. Her temperature fell to 102 F. Her nuchal rigidity was less. She was mentally alert and still covered one eye because of diplopia. Forty thousand units of combined serum was given intramuscularly. A spinal tap was done, and the fluid was less cloudy. The cell count was 196. The application of wet dressings with sulfanilamide to the operative area was continued.

On April 28 the patient was improving; rigidity was lessened, and the diplopia was inconstant. A spinal tap was done and 30 cc. of fluid removed. The cell count was 168; the fluid was clear. The patient began to cough, and there was a patch of diminished breathing in the base of the right lung posteriorly. Poultices were applied, with definite relief. On April 30 the temperature was 102 F. A spinal

tap was done and a clear fluid obtained. There were 72 cells. The application of wet dressings with sulfanilamide was discontinued. There was no nuchal rigidity and no diplopia.

Dosage of Sulfanilamide and Prontosil

Date	Spinal Fluid Cell Count	Hemoglobin (%)	Red Blood Count	White Blood Count	Dose*
April 19	14,000	69	3,680,000	17,000	Prontosil, 30 cc.
April 20	15,000	..	.....	.....	Prontosil, 45 cc. Sulfanilamide, 30 Gr.
April 21	8,600	..	.....	.....	Prontosil, 50 cc. Prontosil, 15 Gr. Sulfanilamide, 0.8%, 20 cc. Sulfanilamide, 10 Gr.
April 22	4,600	..	.....	.....	Prontosil, 45 cc. Prontosil, 60 Gr.
April 23	1,750	..	.....	.....	Prontosil, 40 cc. Prontosil, 20 Gr.
April 24	1,900	..	.....	.....	Prontosil, 10 cc. Prontosil, 60 Gr. Sulfanilamide, 35 Gr.
April 25	4,000	68	3,700,000	16,500	Sulfanilamide, 45 Gr. Prontosil, 15 cc.
April 26	2,400	..	.....	.....	Sulfanilamide, 105 Gr.
April 27	196	68	3,800,000	22,400	Sulfanilamide, 100 Gr.
April 28	184	68	3,300,000	21,000	Sulfanilamide, 100 Gr.
April 29	168	66	3,100,000	19,700	Sulfanilamide, 75 Gr.
April 30	72	65	3,000,000	20,000	Sulfanilamide, 120 Gr.
May 1	76	..	.....	.....	Sulfanilamide, 120 Gr.
May 2	.....	63	3,000,000	.....	Sulfanilamide, 120 Gr.
May 3	50	..	.....	.....	Sulfanilamide, 75 Gr. Prontosil, 15 Gr.
May 4	.....	60	2,800,000	.....	Sulfanilamide, 90 Gr. Prontosil, 45 Gr.
May 5	.....	55	2,300,000 (transfusion)	.....	Sulfanilamide, 35 Gr. Prontosil, 55 Gr.
May 6	.....	60	2,600,000	.....	Sulfanilamide, 30 Gr. Prontosil, 45 Gr.
May 7	.....	60	2,620,000	9,300	Prontosil, 50 Gr.
May 8	.....	60	2,700,000	9,600	Prontosil, 20 Gr.
May 9	2	..	.....	.....	Prontosil, 25 Gr.
May 10	.....	60	2,620,000	.....	Prontosil, 20 Gr.
May 11	.....	60	2,500,000	8,000	Prontosil, 40 Gr.
May 12	.....	..	.....	.....	Prontosil, 30 Gr.
May 13	.....	64	2,900,000	.....	Sulfanilamide, 40 Gr.
May 14	.....	..	.....	.....	Sulfanilamide, 40 Gr.
May 15	.....	..	.....	.....	Sulfanilamide, 40 Gr.
May 16	.....	68	2,900,000	.....	Sulfanilamide, 40 Gr.
May 17	.....	..	.....	.....	Sulfanilamide, 50 Gr.
May 18	.....	..	.....	.....	Sulfanilamide, 15 Gr.
May 19	.....	..	.....	.....	Sulfanilamide, 15 Gr.
May 20	.....	80	3,500,000	8,500	Sulfanilamide, 10 Gr.
May 21	.....	..	.....	.....	Sulfanilamide, 10 Gr.

* Doses of prontosil in cubic centimeters indicate that the 2.5 per cent solution was used; doses in grains refer to the powder.

On May 1 the temperature was 101.8 F. A spinal tap was done and a clear fluid obtained. The cell count was 76 cells. The patient's eyes were swollen, and she complained of pains in the joints, evidently manifestations of serum sickness. These symptoms were controlled by epinephrine.

On May 2 the patient was improving and not complaining. Ventrex capsules [23] were given for anemia. The next day a spinal tap was done. The fluid was clear and under no pressure and contained 50 cells per cubic millimeter.

By May 5 the hemoglobin content had fallen to 55 per cent and the erythrocyte count to 2,300,000. The patient's blood was typed and found to be of type II. Difficulty was encountered in cross matching her blood for transfusion, but a satisfactory donor was finally obtained. Four hundred cubic centimeters of blood was given by the citrate method, after which the patient promptly had a chill lasting twenty minutes. Her temperature rose to 104 F., but by the next day it had fallen to 99.4 F.

Her improvement from then on was steady and rapid. On May 9 a clear fluid was obtained by spinal tap, containing 2 cells per cubic millimeter. On May 18 she was out of bed, and two days later the hemoglobin content was 80 per cent and the erythrocyte count 3,500,000.

She was discharged on May 22, thirty-four days after admission to the hospital, with no residual signs of her meningitis. The operative wound was still open at the lower angle and granulating well.

COMMENT

A case of pneumococcic meningitis with recovery is reported. Growth of the organism was obtained on four occasions from the cultures of spinal fluid.

Despite massive doses of sulfanilamide, no toxic signs were observed except for anemia, which responded favorably to a single blood transfusion and administration of ventrex capsules [23] by mouth.

It is the opinion of the experts that the focus of infection if evident should be eliminated despite the presence of meningitis. In the case presented a purulent frontal sinus was opened externally and continuous wet dressings of sulfanilamide, 0.8 per cent, were applied.

Though the patient had been receiving adequate doses of prontosil [22] and sulfanilamide for six days and her spinal fluid was rendered sterile, she did not appear clinically improved. Her temperature fluctuated between 102 and 105 F.; restlessness, irritability and nuchal rigidity were still present. However, after the intramuscular injection of 40,000 units of type V and VII pneumococcus (horse) serum and the intraspinal injection of a similar amount, her improvement was rapid and apparent. A total of 160,000 units of serum was given.

In the light of Rosenthal's [7] findings that sulfanilamide is bacteriostatic and bactericidal for pneumococcus, it would seem that ideal therapy would consist in destroying the organism (with sulfanilamide) and neutralizing the toxins (with serum).

5722 Fourth Avenue.

23. Ventrex Capsules (Parke, Davis & Co.) contain a preparation of desiccated, iron and ammonium citrates, thiamin chloride and riboflavin.

CONGENITAL ABSENCE OF ONE TONSIL

Microtia and Polydactylism in the Same Patient

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An attack of acute otitis and mastoiditis in a deformed ear brought the patient to the hospital and permitted study of an interesting group of congenital deformities.

REPORT OF A CASE

A pleasant though mentally sluggish little girl of 8 years came to the outpatient department with a history of cold in the head and pain in the left ear of three days' duration. Fever and dizziness had been noted for twenty-four hours. The child looked ill, cried, held her hand to the deformed ear and complained of pain and fulness. Her temperature was 103.2 F. and her pulse rate 96. There was obvious acute nasopharyngitis. Nystagmus and vertigo were absent. The left ear was microtic, with no external canal. However, the mastoid process and the region of the buried cartilaginous canal were tender. While the child was under care in the hospital the acute symptoms quickly subsided, and the opportunity for detailed study of the odd congenital anomalies presented itself.

The left tonsil was absent (fig. 1). The anterior pillar too was missing. This in the presence of an overdeveloped gland on the other side was all the more striking and led to the hasty and erroneous conclusion that a surgical attack had been made on the missing organ. Two points caused reconsideration: 1. A follicle was present in the upper extremity of the empty fossa. 2. The border of the tongue, instead of being bound down to the lateral wall of the pharynx and the fossa by postoperative adhesions, bellied lonesomely into the empty fossa. There was not and apparently never had been any anterior faucial pillar with its palatoglossus muscle. The parents stated that the child had never been submitted to operation and volunteered the information that something "queer" had been noted in her mouth at birth.

The uvula pointed to the sound side. Palatal and pharyngeal movements were normal. The nasopharynx contained a small adenoid; the eustachian tori and the orifices of the tubes were normal. Clinical and roentgen examination of the nose and sinuses revealed normal structure and development. The contour and movements of the mandible were normal. The dental formula was as follows: Rt $\frac{6edc21/12c4e56}{6edc21/12cde6}$. There were miscellaneous malocclusions, including a buccal occlusion of the left lower 6 year molar and an open bite anteriorly. It was felt that these irregularities could not be considered with certainty to have a congenital cause. The palate was of normal bony construction and moderate height and arched.

The Deformed Ear.—The left ear presented one of the many variations of microtia (fig. 2). There was no external opening, but a semblance of a carti-

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From the Montreal General and the Saint Mary's Hospital.

Read at the meeting of the Section of Otolaryngology, Montreal Medico-Chirurgical Society, April 21, 1938.

laginous canal and the edge of the tympanic plate were palpable. The tragus and both roots and the superior curve of the helix were absent. The posterior curve of the helix, the lobule and a conglomeration of skin-covered cartilage representing the antihelix and antitragus could be made out. That is, the superior parts of the pinna, which develop from the tissues of the mandibular arch, were absent, while the inferior parts, formed from the hyoid arch, were present. The cartilage of the meatus, which develops in the tissues between the two arches, was deformed. The right ear was normal and well formed.

The attack of acute otitis and mastoiditis seemed to bear witness that the middle ear and the mastoid were present and the eustachian tube patent. Roentgen studies showed the left mastoid well developed, though not as cellular as the right. On the film the greatest distance of cells from the meatus was 2.25 cm. The

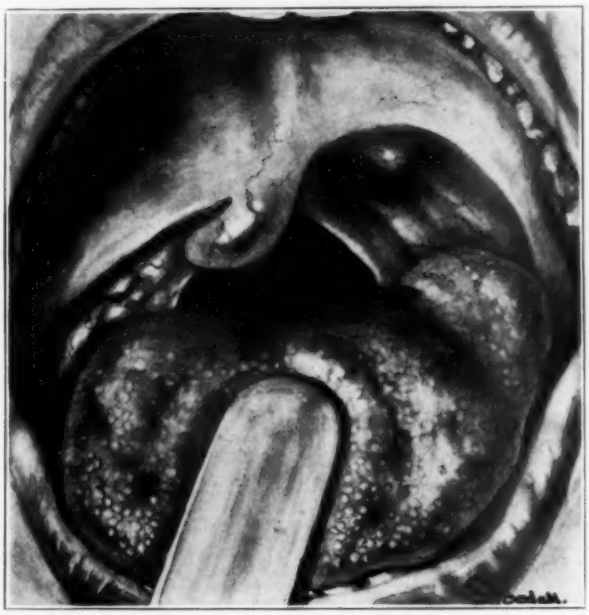

Fig. 1.—Congenital absence of the left tonsil. The uvula points to the sound side. The follicle in the upper extremity of the empty fossa can be seen, as well as the absence of the anterior faucial pillar and of the palatoglossus muscle and the peculiar development of the tongue on the deformed side.

internal auditory meatus appeared normal. These roentgen appearances and the subsequent functional tests pointed to the presence of an intact inner, and a reasonably formed middle, ear.

Vestibular and cochlear tests gave normal results on the sound side. Severe conduction deafness was present on the deformed side. When a noise apparatus was placed in the right ear the conversational voice could be heard when almost in contact with the deformed ear. The Weber test showed lateralization to the left, and the Rinne test on this side showed no abnormality. The audiogram (fig. 3) concurred with these findings, showing a 5 per cent loss of hearing for speech on the sound side and a 53 per cent loss on the deformed side.

The Double Thumb.—The left hand bore two thumbs on a single metacarpal bone (figs. 4 and 5), each having well formed proximal and distal phalanges, somewhat smaller than those of the normal hand. There was a flexion deformity of the radial thumb, and a webbing extended between the two up to the knuckle.

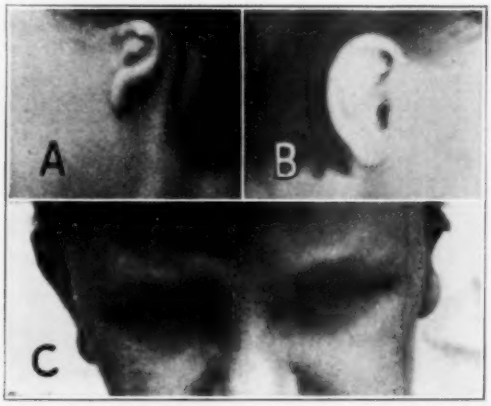

Fig. 2.—*A,* deformed ear. The parts derived from the mandibular arch are missing, while those derived from the hyoid arch are present. *B* shows the normal ear, and *C,* a front view of the patient, illustrating contrast between the two ears.

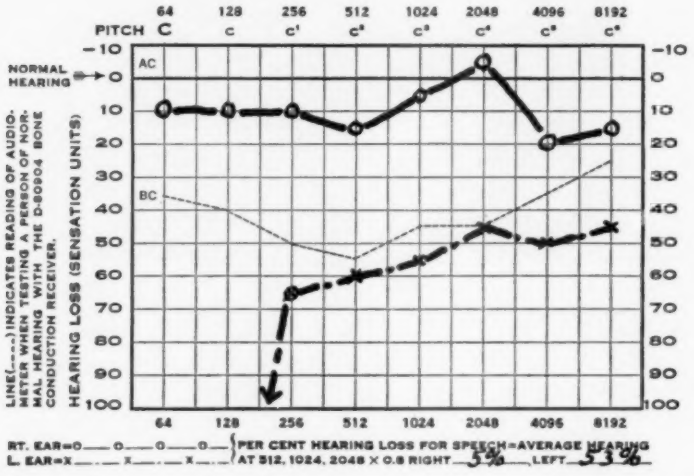
PITCH
64 128 256 512 1024 2048 4096 8192
C c c' c'' c''' c'''' c''''' c''''''
NORMAL HEARING
AC
BC
HEARING LOSS (SENSATION UNITS)
−10 0 10 20 30 40 50 60 70 80 90 100
LINE(—.—.—) INDICATES READING OF AUDIOMETER WHEN TESTING A PERSON OF NORMAL HEARING WITH THE D-80904 BONE CONDUCTION RECEIVER.
RT. EAR=O—.—O—.—O—.—O—.—
L. EAR=X—.—.—X—.—.—X—.—.—X—.—.—
PER CENT HEARING LOSS FOR SPEECH=AVERAGE HEARING AT 512, 1024, 2048 × 0.8 RIGHT 53% LEFT 53%

Fig. 3.—Audiogram, showing loss of perception of low tones and 53 per cent loss of hearing in the deformed ear.

Other Observations.—The only other abnormality was a harsh systolic murmur, best heard over the cardiac apex. There was no cyanosis or clubbing of the fingers. When the history of birth was unearthed, similar findings were seen to be noted there, and the question of congenital heart disease and the possibility of a patent interventricular septum had been mooted.

The child had been born on Jan. 17, 1928, weighing 5 pounds (2,267.96 Gm.), after a ten month gestation. External version and instrumental delivery were resorted to, the mother having spent fifty-two hours in labor. The cord was only 11 inches (28 cm.) long. There was slight asphyxia at birth. The deformities of the ear and hand were noted, and reference was made in the report to an abnormality of the left side of the hard palate and the left tonsillar fossa.

No familial history of congenital deformity could be obtained. At the birth of the child the father's age was 29 and the mother's 26. The patient was the first

Fig. 4.—Polydactylism.

Fig. 5.—Roentgenogram of the deformed thumb.

of 5 children; among the others no congenital abnormalities could be found. There were twin boys aged 6, a boy aged 4 and a girl aged 1½ years.

These findings would seem to be at variance with those of most authors who have been seeking rhyme or reason in congenital deformity.

1414 Drummond Street.

RECOVERY FROM HEMOLYTIC STREPTOCOCCIC MENINGITIS OF OTITIC ORIGIN

W. S. Gonne, M.D.; M. W. Michels, M.D., and T. Watson, M.D., Detroit

Since the advent of sulfanilamide, an increasing number of cases of hemolytic streptococcic meningitis with recovery have been reported. We feel that such cases, however, are of sufficient interest and significance to justify adding this present case to the series.

Gray,[1] in a comprehensive review of the literature, listed 66 cases of streptococcic meningitis with recovery in the period from 1901 to 1935. Trachsler [2] found 39 additional instances of recovery in the short interval following the introduction of sulfanilamide; he reported 5 original cases.

The experimental work of Domagk [3] and later of Long [4] showed the value of chemotherapy in the treatment of streptococcic infections and provided an impetus for much of the later work. Long found little evidence that sulfanilamide was bactericidal; however, bacteriostasis of hemolytic streptococci was found to occur in mediums containing sulfanilamide. The action of the drug has been considered primarily one of slowing down the rate of multiplication of the streptococci. Mellon,[5] as a result of his experimental studies, decided that there was no indication of phagocytosis in the mechanism of the therapeutic action of the drug.

Despite the favorable action and the rapid response so often noted after the institution of adequate sulfanilamide therapy, other fundamental practices must be carried out if a successful outcome is to be achieved. Early surgical intervention is often desirable in cases in which there are obvious foci. Adequate drainage of the spinal fluid is important, as well as repeated small blood transfusions. Adjuvant procedures must be individualized as the case demands.

REPORT OF A CASE

F. H., a 9 year old white girl, was admitted to the Children's Hospital of Michigan at 12:05 a. m. on Feb. 26, 1938. Projectile vomiting had occurred a

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From the Department of Otolaryngology, Children's Hospital of Michigan.

1. Gray, H. J.: Streptococcic Meningitis, J. A. M. A. **105**:92 (July 13) 1935.

2. Trachsler, W. H.; Frauenberger, G. S.; Wagner, C., and Mitchell, A. G.: Streptococcic Meningitis, with Special Emphasis on Sulfanilamide Therapy, J. Pediat. **11**:248 (Aug.) 1937.

3. Domagk, G.: Ein Beitrag zur Chemotherapie der bakteriellen Infektionen, Deutsche med. Wchnschr. **61**:250 (Feb. 15) 1935.

4. Long, P. H., and Bliss, E. A.: Observations on the Mode of Action of Sulfanilamide, J. A. M. A. **108**:1523 (Nov. 6) 1937.

5. Mellon, R. R.; Gross, P., and Cooper, F. B.: Experimental Studies with Sulfanilamide and with Prontosil, J. A. M. A. **108**:1855 (May 29) 1937.

few hours prior to her admission. She complained of intense frontal headache and photophobia, which had been present for one day. The temperature was elevated to 103.8 F. on admission.

History.—The patient had had a tonsillectomy twelve days prior to the illness reported here. Nine days after this operative procedure she had complained of pain in the left ear, severe generalized headache and backache, which was not relieved by acetylsalicylic acid. Irritability, restlessness and general malaise had increased up to the time of admission.

She had been seen in the outpatient department on Oct. 11, 1937, presenting chronic suppurative otitis media and mastoiditis on the left side of five years' duration. There was considerable foul débris in the external canal, removal of which revealed a central perforation of the drum head. The right drum head was intact. Simple mastoidectomy and removal of hypertrophied tonsils and adenoids were advised. In view of the chronicity of the disease, it was thought that more extensive surgical intervention in the mastoid region would probably be necessary in the future. Roentgenograms of the mastoids showed a normal right mastoid of the adult type and sclerosis of the petrous portion of the temporal bone on the left, with some added density in the peripheral portion but no frank destruction. The parents objected to mastoidectomy, preferring to temporize with tonsillectomy.

The patient's early infancy and childhood had been normal, except that she had had measles at 4 years, complicated by otitis media on the left side, and pneumonia at 7 years. The family history was essentially noncontributory.

Physical Examination.—Examination showed an acutely ill girl of 9 years, well developed and of good nutrition. She was irritable and complained repeatedly of severe frontal headache; however, she was rational and coherent. Her head was held in a stiff fashion, with definite nuchal rigidity. She resented any changes in position. The pupils were moderately dilated but reacted normally. There was no limitation of extraocular movements, and no nystagmus was noted. Funduscopic examination revealed well demarcated disks, with no increased tortuosity of the veins. Examination of the ears revealed a foul-smelling purulent discharge in the left external canal; no postauricular edema was present. Pain on palpation was present over the left mastoid tip. The right drum head was intact and of normal luster. There was no tenderness over the paranasal sinuses. The throat still showed a grayish membrane of a recent tonsillectomy over the right fossa. No facial asymmetry was noted. Examination of the chest showed a suppression of breath sounds over the right upper lobe. The cardiac rhythm was normal; the point of maximum impulse was in the fourth interspace. No murmurs were heard. While the abdomen was tender on palpation, no rigidity or masses were encountered. The liver and spleen were not palpable. Neurologic examination demonstrated positive Kernig and Brudzinski signs. Superficial and deep reflexes were present; Babinski's sign was negative. Tests of cerebellar function were negative.

Clinical Course.—Culture of the blood and lumbar tap were performed on admission. The latter revealed a fluid under increased pressure, with 2,530 cells, 90 per cent polymorphonuclears, a 2 plus reaction to Pandy's test, 21 mg. of sugar per hundred cubic centimeters and a total of 175 mg. of proteins per hundred cubic centimeters. Roentgen examination demonstrated a sclerosing process in the left mastoid, with no residual cellular structure; the right mastoid had a normal appearance. Roentgenograms of the chest showed a little prominence of

the hilar markings but no evidence of parenchymal disease in either lung. The sudden onset of meningitis, in view of the history and findings, was considered of probable otitic origin. Early exenteration of the left mastoid seemed advisable.

Operation.—The patient was given 350 cc. of 10 per cent dextrose in saline solution intravenously prior to operation. Eleven hours after admission complete mastoidectomy was performed on the left side with the patient under anesthesia induced by nitrogen monoxide and oxygen. The mastoid cortex was found to be hard and sclerotic. A destructive process was encountered near the antrum, which extended along the inner table overlying the middle fossa. Numerous granulations were present but no free pus noted. Pneumatization occurred near the tip. A limited area of caries was present in the solid angle. The area from the zygoma to the sinudural angle was completely uncovered. The dura in this region was hyperemic and congested, bulging readily into the area of decompression. The sigmoid sinus was uncovered over the knee; the dura was normal, with no granulations. After complete exenteration of the mastoid, the cavity was cleansed and packed lightly with petrolated iodoform gauze. The face was intact on reacting.

Postoperative Course.—Cultures of spinal fluid revealed gram-positive cocci in short chains twelve hours after inoculation on nutrient agar mediums. Interstitial administration of sulfanilamide, 1 grain per pound (0.14 Gm. per kilogram) daily was instituted. It was combined with lactate-Ringer (Hartmann's) solution to decrease acidosis. In view of the projectile vomiting and toxemia, parenteral fluids were administered freely. During the day of operation, the patient's condition remained critical. She complained of intense generalized headache and pain in the extremities. Projectile vomiting continued. On the following day, she was restless, irrational and comatose. Nuchal rigidity remained, but there were no new neurologic findings. Lumbar puncture showed a cloudy fluid with 2,300 cells, 90 per cent polymorphonuclears, a 4 plus reaction to Pandy's test, 14 mg. of sugar per hundred cubic centimeters and 180 mg. of protein per hundred cubic centimeters. The culture of the spinal fluid was again reported positive for the hemolytic streptococcus.

On February 28 the level of sulfanilamide in the blood was 20 mg. per hundred cubic centimeters (according to the method described by Marshall [6]). The patient became incontinent of urine and continued to have emeses. The following day she showed a definite improvement. She was alert and rational and was able to take some fluids orally. A rather marked cyanosis of the lips and nail beds was present, but administration of sulfanilamide was continued. Kernig's and Brudzinski's signs remained positive. Improvement continued, and on March 3 rigidity of the neck was absent for the first time. No muscular weaknesses were evidenced. During the ensuing week, excellent progress was made. Check-up roentgenograms of the petrous pyramids taken on March 5 showed no pneumatization of either apex and no indication of destruction. A series of transfusions of 125 cc. of citrated blood was administered. Lumbar puncture showed 100 cells, 22 per cent polymorphonuclears, 48 mg. of sugar per hundred cubic centimeters and 140 mg. of proteins per hundred cubic centimeters.

The level of sulfanilamide in the blood on March 7 was 14.6 mg. per hundred cubic centimeters. The temperature curve, which previously had been of the picket fence type, tended to flatten out. The dose of sulfanilamide was gradually

6. Marshall, E. K.; Emerson, K., Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide, J. A. M. A. **108**:953 (March 20) 1937.

diminished, and administration was discontinued on March 11. The child was sitting up in bed at this time, with no subjective complaints. The left middle ear was still discharging freely, and the mastoidectomy wound remained open. After a satisfactory week, of normal temperature and regular pulse, she was discharged to the outpatient department for further observation.

The mastoidectomy wound was completely healed on March 28; however, the middle ear was still discharging moderately. This discharge continued for one week. The child was checked at the one month interval, at which time she was participating in all childhood activities. A check-up blood count showed no depletion that could be attributed to the use of sulfanilamide. The left drum head still presented a fairly large perforation. The whispered voice was heard at 8 feet (244 cm.) in the affected ear. The patient was reexamined on May 21, when no positive findings or sequelae of her meningitis were noted.

Summary of Treatment.—The treatment may be summarized as follows:

February 26, 1938:

2:30 a. m.	Lumbar puncture
10:00 a. m.	Intravenous administration of dextrose, 350 cc., 10 per cent in saline solution
11:35 a. m.	Mastoidectomy on left
2:15 p. m.	Intravenous administration of dextrose, 350 cc., 10 per cent in saline solution; blood culture
6:00 p. m.	Sulfanilamide, 1.6 Gm. in 200 cc. of saline solution, with 8 cc. of lactate-Ringer (Hartmann's) solution, administered interstitially
9:00 p. m.	Intravenous administration of dextrose, 350 cc., 5 per cent in saline solution
12:00 m.	Sulfanilamide, 1.6 Gm. in 200 cc. of saline solution, with 8 cc. of lactate-Ringer (Hartmann's) solution, administered interstitially

February 27, 1938:

8:00 a. m.	Sulfanilamide, 1.6 Gm. in 200 cc. of saline solution, with 8 cc. of lactate-Ringer (Hartmann's) solution, administered interstitially
9:00 a. m.	Intravenous administration of dextrose, 350 cc., 5 per cent in saline solution
4:00 p. m.	Sulfanilamide, 1.6 Gm. in 200 cc. of saline solution, with 8 cc. of lactate-Ringer (Hartmann's) solution, administered interstitially; intravenous administration of dextrose, 350 cc., 5 per cent in saline solution
6:00 p. m.	Lumbar puncture
10:00 p. m.	Sulfanilamide, 1.6 Gm. in 200 cc. of saline solution, with 8 cc. of lactate-Ringer (Hartmann's) solution, administered interstitially

February 28, 1938:

4:00 a. m.	Sulfanilamide, 1.6 Gm. in 200 cc. of saline solution with 8 cc. of lactate-Ringer (Hartmann's solution) administered interstitially
9:00 a. m.	Intravenous administration of dextrose, 350 cc., 5 per cent in saline solution

10:30 a. m. Sulfanilamide, 1.6 Gm. in 200 cc. of saline solution, with 8 cc. of lactate-Ringer (Hartmann's) solution, administered interstitially

4:00 p. m. Intravenous administration of dextrose, 350 cc., 5 per cent in saline solution

March 1, 1938:

Intravenous administration of dextrose, 350 cc., 5 per cent in saline solution; sulfanilamide and sodium bicarbonate, 1 Gm. of each, administered orally every 6 hours; transfusion of 125 cc. of citrated blood.

March 2, 1938:

Transfusion of 125 cc. of citrated blood

March 3, 1938:

Transfusion of 125 cc. of citrated blood; amount of sulfanilamide and sodium bicarbonate reduced to 1 Gm. of each three times a day

March 5, 1938:

Lumbar puncture

March 9, 1938:

Sulfanilamide and sodium bicarbonate, 0.6 Gm. of each, three times a day

March 11, 1938:

Administration of sulfanilamide discontinued

Laboratory Data.—The laboratory data are as follows:

Spinal Fluid

Date	Cells, per Cu. Mm.	Polymorphonuclears, %	Lymphocytes, %	Reaction to Pandy's Test	Sugar, Mg. per 100 Cc.	Protein, Mg. per 100 Cc.
2/26/38	2,530	90	10	++	21	175
2/27/38	2,300	90	10	++++	14	180
3/ 5/38	100	22	78	0	48	140

Blood

Date	Hemoglobin, Gm.*	Red Blood Cells	White Blood Cells	Polymorphonuclears, %	Small Lymphocytes, %	Large Lymphocytes, %	Mononuclears, %
2/26/38	12	4,000,000	20,000	85	15	..	..
3/ 4/38	13	5,200,000	15,000	86	14	..	..
3/ 9/38	12	3,700,000	8,450	64	34	..	2
4/ 3/38	11.5	3,450,000	11,900	60	28	12	..

Sulfanilamide Levels

2/28/38	Blood	20 mg. per hundred cubic centimeters
3/ 2/38	Blood	17.8 mg. per hundred cubic centimeters
3/ 5/38	Spinal fluid	14 mg. per hundred cubic centimeters
3/ 7/38	Blood	14.6 mg. per hundred cubic centimeters

Cultures

			Mediums
2/26/38	Blood	Negative (7 days)	Beef hormone broth
2/26/38	Left mastoid	Hemolytic streptococci	Chocolate agar
2/26/38	Spinal fluid	Hemolytic streptococci	Nutrient agar and chocolate agar
2/27/38	Spinal fluid	Hemolytic streptococci	Nutrient agar and chocolate agar
3/ 5/38	Spinal fluid	Negative	Nutrient agar and chocolate agar

* Hemoglobin determinations by the Sahli method.

SUMMARY AND CONCLUSIONS

A case of hemolytic streptococcic meningitis in a girl of 9 years is presented. Purulent otitis media had been present for five years before

meningeal symptoms developed. Two successive lumbar punctures showed hemolytic streptococci on culture. Cultures of material from the mastoid after early exenteration with wide exposure of the dura of the middle fossa also showed hemolytic streptococci. Sulfanilamide therapy was promptly instituted. A total of 42 Gm. of sulfanilamide was administered during a thirteen day interval (patient's weight 26 Kg.). Supportive parenteral fluids and small blood transfusions were given.

Prompt subsidence of symptoms and clinical findings followed sulfanilamide therapy. Aside from transient cyanosis, no complications attributable to the sulfanilamide were observed. Acidosis was prevented by the use of lactate-Ringer (Hartmann's) solution and sodium bicarbonate. The patient was discharged on the nineteenth day. The subsequent course was entirely uneventful.

AGRANULOCYTOSIS ASSOCIATED WITH MAXILLARY SINUSITIS

THEODORE E. WALSH, M.R.C.S., L.R.C.P., CHICAGO

Agranulocytosis (secondary granulopenia) occurs occasionally in the course of a prolonged infection. It has been reported in association with streptococcic pneumonia, osteomyelitis and staphylococcic septicemia. It is uncommon, however, to find malignant neutropenia occurring as a complication of maxillary sinusitis.

REPORT OF A CASE

M. E. D., a single white woman aged 39, a stenographer, was admitted to the Albert Merritt Billings Memorial Hospital to Dr. O. H. Robertson's medical service on March 13, 1938. She complained of pain in the right side of the chest that had been present for one day and of having had a chill on the day before admission.

Of significance in her past history was an attack of pneumonia in 1935, with a stormy course and delirium; she was, however, in a hospital for only eighteen days at that time. She gave a history of frequent colds (four or five a year) but no history of sinusitis. During the week prior to admission to the hospital she had had a cold and had taken a total of 4 grains (0.26 Gm.) of codeine in that time. She had taken also guaiacol carbonate, a total of 25 grains (1.62 Gm.), during the same time. She had taken no aminopyrine or barbiturates.

On admission the patient appeared weak and ill and had a slight cough without expectoration. Physical examination revealed no disease. The lungs were normal to percussion and auscultation; there was no friction, and the diaphragms moved well on both sides. There was no nasal obstruction or discharge. The roentgenograms of the chest showed normal lungs.

On March 14 the leukocyte count was 2,600, and there were no granulocytes. A transfusion of whole blood (550 cc.) was given, and medication with extract of yellow bone marrow was started, the patient receiving 150 drops on March 14 and 200 drops each day thereafter until March 21. In spite of this treatment the leukocyte count remained between 2,260 and 2,700, and the proportion of granulocytes ranged between 0 and 25 per cent until March 20.

Roentgenograms of the nasal sinuses were taken on March 17 and showed complete clouding of the left antrum. The right antrum was half full of fluid. The ethmoid sinuses appeared partly cloudy.

I saw the patient in consultation on March 19, and at that time the nose and throat appeared normal. I washed both antrums through the normal ostium and obtained pus from both. On March 20 the leukocyte count was 4,850, and on March 21, 6,000. The antrums were washed on March 21, 24 and 28, no pus being obtained on the last occasion. The leukocyte count and the percentage of granulocytes increased until the patient was discharged from the hospital on March 28, with a leukocyte count of 8,000 and 52 per cent granulocytes.

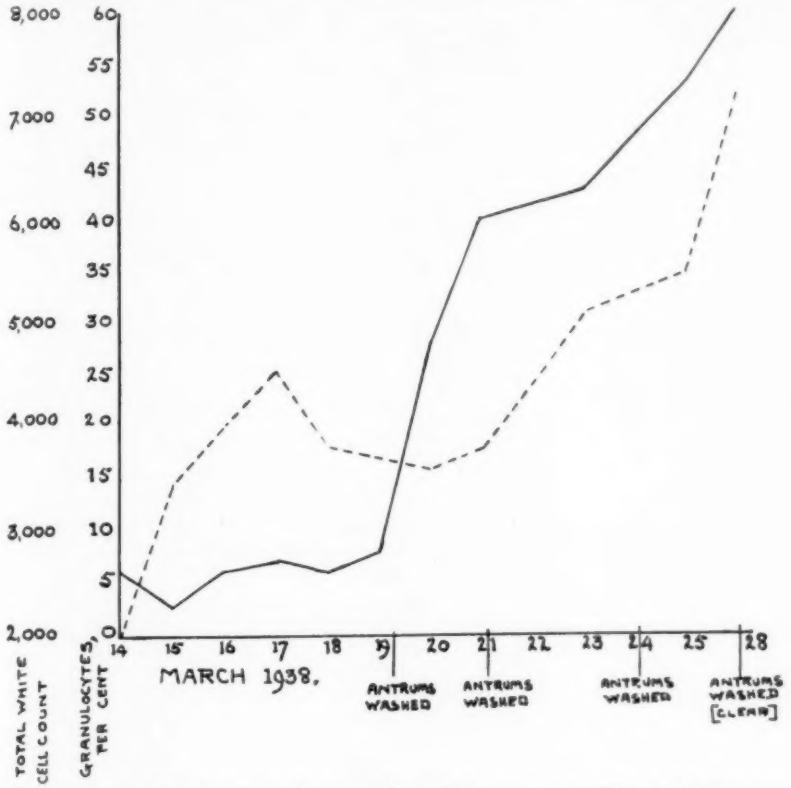
From the Department of Surgery, Division of Otolaryngology, University of Chicago.

Cultures of the pus from the sinuses showed the infecting organism to be Streptococcus viridans.

The patient returned to her work early in April and has been well since. She was last seen by me on May 20, when the sinuses were clear and the leukocyte count was 9,300 with 57 per cent granulocytes.

COMMENT

It is of interest that a severe infection of the maxillary sinuses was present in this case with so little clinical evidence of its existence. The



Change in the blood count after washing of the antrums. The solid line represents the total white cell count; the broken line, the percentage of granulocytes. Yellow bone marrow extract was given by mouth, 200 drops a day, from March 14 to March 22 inclusive.

persistent unproductive cough in the presence of a mild cold was suggestive of sinal infection, but the absence of signs in the nose or throat was unusual.

The change in the blood count after washing of the antrums is noteworthy. It has been claimed that extract of yellow bone marrow will cause an increase in the leukocyte count after forty-eight hours. In this case, as is graphically shown in the chart, there was no increase in the number of leukocytes in spite of medication with yellow bone

marrow in adequate doses for six days. The increase in the number of leukocytes and in the percentage of granulocytes after the evacuation of the antrums and the return of the blood count to normal when the antrums were clear point to the sinal infection as the cause of the disease in this case.

The infecting organism in this case was Str. viridans. Streptococci are the organisms most commonly found associated with agranulocytosis, but the disease cannot be reproduced in animals by bacterial inoculations.

I am indebted to Dr. O. H. Robertson for permission to publish this case and to Dr. Ernestine Kandel, in whose laboratory all the blood counts were done.

Abstracts from Current Literature

Ear

AUDIOMETERS AND HEARING AIDS A. A. HAYDEN, J. A. M. A. **110**:723 (March 5) 1938.

Hayden briefly discusses the value of the audiometer and the types of hearing aids that are most commonly used. The construction of the transmitter can be so altered that the sound can be "peaked" or intensified to fit approximately the loss of hearing shown on the audiogram.

The author wisely states that the method by which the vacuum tube works in the audiometer, the amplification of sound, the workings of the attenuator, the definition of bel and decibel and similar matters pertaining to the audiometer and the hearing aid require knowledge so technical that it is best to leave them to the Bureau of Standards, the American Standards Association and the Council on Physical Therapy of the American Medical Association and to the professional associates and designated consultants.

In his tests, 30 patients had audiometric studies performed by three experienced observers. They were given rest periods to minimize the confusion due to fatigue of both the patient and the observer. Four audiometers of different makes were used. Fourteen of the patients were found to have losses greater than the Western Electric 2-A audiometer could measure, so that their audiograms were discarded. He came to the following conclusions: Despite the variations, audiometers furnish the best means of testing hearing acuity; any one of the four audiometers tested gives more useful information to the otologist than any other now available; the lack of purity of the sound waves apparently did not introduce any serious error that could not be explained largely by other causes; the need for a sound-proof room increases as the loss of hearing to be tested decreases, though a quiet room is always essential, and, finally, an audiometer should be part of the office equipment of every otologist.

GORDON, Philadelphia.

ON BONE FORMATION IN SCALA TYMPANI OF OTOSCLEROTICS. F. R. NAGER and J. S. FRAZER, J. Laryng. & Otol. **53**:173 (March) 1938.

The changes in otosclerosis are generally confined to the labyrinthine capsule, while ordinarily the inner ear shows only minor alterations. Histologic examination of the petrosae in many cases of otosclerosis, however, disclosed some rare instances in which there was more or less extreme bone formation in the scala tympani, and it is with such changes that the authors are concerned. Six cases in which these changes were present in the scala tympani are reported. In all the cases there were characteristic symptoms of advanced stages of the disease, but in none was there any symptomatic peculiarity to suggest that involvement of the inner ear had taken place. Except in case 2, in which the round window was free, histologic examination showed marked otosclerotic processes about both windows. This was to be expected, but new bone formation was found in the scala tympani at the basal turn in cases 1, 2, 4, 5 and 6, while in case 3 the cochlear changes were found near the round window. It is supposed that the bone formation in the scala tympani is due to irritation by the otosclerotic process in the labyrinthine wall.

LE JEUNE, New Orleans.

USE OF THE MAYER POSITION IN THE ROENTGENOGRAPHIC EXAMINATION OF THE EAR IN THE NEWBORN. P. BÈTOULIÉRES, Rev. de laryng. **59**:16 (Jan.) 1938.

There are three positions commonly used in the roentgenographic examination of the ear. These are the position of Schüller (similar to the American position of Law), that of Stenvers and that of Mayer. The author says the Schüller position is useless for the young child, for Granger's sign does not appear until there has been mass destruction of bone. The author's technic for the Mayer position is as follows: The child is placed in the dorsal decubitus. The head is placed in flexion and rotated to the side being examined, so that the sagittal plane makes an angle of 45 degrees with the horizontal plane. The film is placed flat under the ear being examined. The incident ray enters the cranium through the frontal boss of the opposite side and is directed to the external auditory canal of the side being examined. This causes the central ray to enter at an angle of 45 degrees to the horizontal, i. e., in American roentgenologic parlance, "45 degrees toward the feet." The position is said to be readily accomplished, and the exposure is made in one fiftieth of a second. Excellent illustrations showing the position and the roentgenograms obtained accompany the article. In the roentgenograms the following are clearly visualized: the semicircular canals, the petrous portion of the temporal bone, both internal and external to the labyrinth, the ossicles and, most important, the detailed anatomy of the antrum tympanicum. The author believes that for the young child the examination in the Mayer position is the examination of choice.

BATSON, Philadelphia.

SUPPURATIVE CHONDRITIS OF THE EAR TREATED WITH ROENTGEN RAYS. F. BONNET-ROY, P. GRIPPON DE LA MOTTE and DRENEAU, Rev. de laryng. **59**:97 (Jan.) 1938.

A patient was given a total of 1,500 r (roentgens) in divided doses. Five treatments, one week apart, with 300 r per treatment, with filtration, were used. Favorable results were obtained. The authors emphasize that while others have treated simple othematoma with roentgen rays, the condition was complicated by infection in their case.

BATSON, Philadelphia.

TUBERCULOSIS OF THE MASTOID PROCESS: DEATH DUE TO SUDDEN HEMORRHAGE FROM THE INTERNAL CAROTID ARTERY. ROUX, Rev. de laryng. **59**:103 (Jan.) 1938.

In a case of generalized tuberculosis, there was a localized tuberculous lesion in the left mastoid process. In spite of adequate surgical drainage the lesion did not regress, and death occurred as a result of massive hemorrhage from the internal carotid artery.

BATSON, Philadelphia.

OTITIS MEDIA AND VITAMIN C. M. BAER, Rev. de laryng. **59**:165 (Feb.) 1938.

The author feels that in 15 cases of otitis media the patients were suffering from a deficiency of vitamin C and further believes that administration of this vitamin favorably influenced the course of the condition.

BATSON, Philadelphia.

ROENTGENOGRAPHIC STUDY OF THE EUSTACHIAN TUBE. ERNEST HEIMENDINGER, Rev. de laryng. **59**:303 (March) 1938.

Roentgenography of the eustachian tube was first done by Portmann, Retrouvey and Lachapele, who worked on the cadaver, using mercury and mercury amalgams. The pharyngeal orifice of the eustachian tube in the lateral view corresponds to the anterior half of the sigmoid notch. It lies on the lower border of the notch at the anterior end, and at its upper portion it corresponds to a horizontal line passing through the middle part of the notch. The cartilaginous tube is readily

depicted when its lumen is filled with opaque material. The osseous portion is seen with more difficulty, for it is overlapped by the heavy petrous bone; however, its conical form can be perfectly distinguished. The isthmus is projected a little below the temporomandibular joint. The eustachian tube has a marked obliquity. In general, it forms with the zygomatic arch an angle of from 30 to 40 degrees opening anteriorly. The bony tube makes an angle with the cartilaginous tube opening below and forward. The apex of the angle corresponds to the isthmus.

There are significant technical difficulties in the roentgenography of the tube in the living. Radiopaque bougies made of silk, rubber and bismuth salts are employed. They are readily sterilized and conform to the tube. The caliber is important. The author uses not over a no. 6 F or 7 F. The bougie is introduced in the usual manner, a large metal eustachian catheter being used, which is removed before the roentgenogram is made. By a series of roentgenograms of the normal subject the accuracy of Portmann's observations were demonstrated. The first films are made to give a lateral and a posteroanterior view. The first view is made with the head in the so-called nose-forehead position. The lateral view is augmented when necessary with films made in the Schüller (similar to the American Law) position. For the final view Hirtz's vertex-chin-film position is used.

This method permits exact localization of strictures in the tube and allows the progress of a condition to be followed. It is to be hoped the method will develop to allow an exact diagnosis of the nature of these strictures. Iodized oil has been tried, but difficulty is experienced in confining it to the tube.

BATSON, Philadelphia.

ANAPHYLAXIS OF ANIMALS PRODUCED BY MEANS OF MICROBES AND HISTOLYSATES OF THE HUMAN EAR. P. P. SMIRNOV, Acta oto-laryng. **26**:12, 1938.

This report by Smirnov is based on two series of experiments designed to obtain sensitization of guinea pigs with products derived from the ears of patients with acute suppurating otitis and mastoiditis. In the first series of experiments sensitization was attempted by means of Staphylococcus aureus which was found in the pus of patients; in the second series, by means of histolysates prepared from tissues excised at the level of the mastoid apophyses of the same patients at the time of trepanation of these apophyses. Anaphylactic shock was obtained only after the injection of the extracts of staphylococci. The reinjection of the intact but killed microbes did not produce anaphylactic shock. Sensitization of the guinea pigs was not obtained by the hystolysates prepared from tissue according to the pepsin method. On the other hand, the histolysates prepared with the same tissues (filtered with the Leitz filter and thus containing no microbes) possessed a toxic action from the first injection practiced on the animals.

EDITOR'S ABSTRACT.

Larynx

TREATMENT OF ASPHYXIAL STATES BY TRACHEOBRONCHIAL STIMULATION. HENRI LEWENFISZ, Rev. de laryng. **59**:311 (March) 1938.

In May 1927 the author reported a series of cases in which normal respiration did not supervene after tracheotomy and the usual methods of artificial respiration. In a case of dyspnea secondary to cancer of the larynx the tracheotomy was technically difficult and slow. The patient did not breathe spontaneously even after the stimulation of artificial respiration. To search for the difficulty a bronchoscope was introduced through the tracheotomy opening. The irritation of the mucous membrane of the bifurcation reflexly provoked respiration.

This experience has been satisfactorily repeated. The author believes that normally the air striking the mucous membrane of the tracheobronchial tree provides the necessary stimulation of the vagus nerve.

He has elsewhere recorded the respiratory curves of animals during experimental bronchoscopy. In one group of animals he used chloralose as a general anesthetic and cocaine as a local anesthetic for the upper respiratory passages; and in another group of animals he practiced cocainization of the upper and the lower part of the respiratory tract. He employed superior and inferior bronchoscopy.

When anesthesia was induced by intravenous administration of chloralose, the modification of the respiratory curve began with the introduction of the bronchoscope into the larynx. The respiration slowed or ceased in expiration. Supplementary stimulation of the mucous membrane of the larynx with a sound produced further slowing or increased the duration of the apnea. There were also marked disturbances of respiratory rhythm. When the bronchoscope had passed the larynx, the respirations were accelerated and deepened by stimulating the tracheal bifurcation with a sound.

The respiratory rhythm was not altered by introducing a bronchoscope directly into the trachea without passing it through the larynx.

In the second group of experiments on dogs under anesthesia induced by chloralose, the mucous membrane of the pharynx and larynx was anesthetized with a 10 per cent solution of cocaine. The introduction of the bronchoscope caused no disturbances of respiration. When the bronchoscope was introduced so far as to irritate the mucous membrane of the bifurcation, the respirations were quickened and deepened.

After cocainization of the mucous membrane of the superior and the inferior part of the respiratory tract the introduction of the bronchoscope did not produce any alterations in respiratory rhythm. Sectioning of the vagus nerve caused a total disappearance of these modifications of the respiratory curve. Suspension of respiration due to stimulation of the mucous membrane of the superior part of the respiratory tract can be combated by stimulation of the mucous membrane of the inferior part.

BATSON, Philadelphia.

LARYNGOTRACHEOPLASTY BY MANGOLDT'S METHOD. A. LASKIEWICZ, Rev. de laryng. **59**:463 (May) 1938.

If a small tracheal fistula does not close spontaneously, closure can be induced by freshening the edges and using simple sliding grafts. After destruction of several tracheal rings and especially after partial destruction of the cricoid cartilage, the closure must be effected by using some denser material, such as aponeurosis, cartilage or bone. Hohmeier, Munich and Lukas suggested the use of fascia lata in 1890. König closed the fistula with a fragment from the external plate of the cricoid cartilage. Rethi used cartilage from the ninth and the tenth rib in a pedicle graft. The cartilages tend to become absorbed, and the soft tissues draw in on deep inspiration. In an effort to remedy this defect, substances such as paraffin, a network of silver wire and sheets of horn on celluloid (Henschen) have been put between the layers. The results have been uncertain, and the procedures have given way to the use of bony grafts.

Schimmelbusch first reconstructed the anterior wall of the trachea with a pedicle skin flap from the jugular notch and reenforced it with a lamina of bone from the sternum. Killian took a long flap and used the lower part of the sternum. Other procedures have endeavored to make use of bone from the clavicle. Pfeiffer and others have used free osteoperiosteal implants in the margins of the fistula and have later carried out plastic procedures.

Mangoldt, in 1900, perfected a method for implanting bits of bone and cartilage with their membranes in the immediate vicinity of the fistula. A portion of costal cartilage with its perichondrium or a piece from the tibia with its periosteum is placed in a subcutaneous pocket formed parallel to and at a little distance from the tracheal fistula. After four to six weeks a cutaneous flap including this implant is cut to exact size, turned into position and attached to the freshened edges. The raw surfaces are then covered by Thiersch grafts and by flaps from the side of the neck.

BATSON, Philadelphia.

Nose

LOW-GRADE FEVER, THE RESULT OF NASOPHARYNGEAL INFECTION. T. P. O'CONNOR, Laryngoscope **48**:38 (Jan.) 1938.

O'Connor says that patients suffering from long-continued low grade fever and fatigue often present a problem baffling for the diagnostician and that such cases of obscure fever are not rare. Fifty-nine patients who came under the author's observation during the last three years presented such symptoms. Most of these patients were referred by physicians as having fever and fatigue which had run a prolonged course without at any time presenting symptomatic, clinical or laboratory features which warranted a definite diagnosis. Three of these patients were relieved of the symptoms after the removal of abscessed tonsils; 1 recovered from the low grade fever after a mastoidectomy was performed, and the remaining 55 were found to have nasopharyngeal infections and no other significant abnormality. Cultures of material taken from the area revealed the presence of large numbers of some pathogen in most of the cases. Treatment of the nasopharynx resulted in eradication of the focus and relief of symptoms in approximately 80 per cent of the cases.

EDITOR'S ABSTRACT.

ANATOMIC CONSIDERATION OF THE DEVELOPMENT OF THE FRONTAL SINUS. BONNAFOUR, Rev. de laryng. **59**:99 (Jan.) 1938.

The author reports 2 cases of pansinusitis with almost identical symptoms. In 1 case, however, there was extensive pneumatization of the frontal sinus. The cells extended two thirds of the distance to the hair line and laterally to the orbital margins. In the other case the frontal sinus was totally absent. The author admonishes that adequate roentgen examination should be made in all cases in which surgical intervention is contemplated.

BATSON, Philadelphia.

UPPER RESPIRATORY PASSAGES OF BAKERS. A. RADZYMINSKI, Rev. de laryng. **59**:174 (Feb.) 1938.

Flour causes irritation of the nasal membranes of bakers and produces chronic hypertrophy of the mucosa, which interferes with nasal breathing, and as a result the flour dust produces irritation of the pharynx and the larynx. The large number of malignant tumors of the larynx observed in bakers and millers may be due to the irritating action of this dust penetrating directly to these parts without the filtering action of the nose. Those seeking to enter the baking and milling trades should have not only a general physical examination but a competent rhinologic examination.

BATSON, Philadelphia.

PATHOLOGICOANATOMIC AND CLINICAL COMMENTS ON A CASE OF CYLINDROMA OF THE NASAL WALL. J. VERNIEUWE and N. GOORMAGHTIGH, Rev. de laryng. **59**:289 (March) 1938.

The authors confirm the malignant nature of cylindroma of the nasal fossa and of the sinuses. Metastases are rare. They feel that the tumor is radiosensitive. The histologic picture and the possible mode of transformation of the structure are discussed, and the authors conclude with Masson: "Cylindromas are tumors of variable malignancy."

BATSON, Philadelphia.

TRANSILLUMINATION WITH THE TISSUES UNDER PRESSURE. EMMANUEL CORNET, Rev. de laryng. **59**:315 (March) 1938.

The author compresses the tissues beneath the eyes with a glass tongue depressor when transilluminating the maxillary sinuses. He places the depressor

horizontally along the inferior orbital margin, pushes in the lower lid and then rotates the glass so that its flat surface compresses the skin.

1. If the results of ordinary transillumination are negative and this method makes them more negative, there is no sinusitis.

2. If the results are negative and this method brings out slight differences in illumination, congestive or edematous sinusitis is present.

3. If the results are slightly positive and this method makes them negative, there is abnormal thickness of bone or skin, congestive sinusitis or a draining, purulent condition.

4. If the results are positive and this method makes them more or less negative, a hyperplastic or cystic condition is indicated.

5. If the results are positive and continue to be so under this method, frank suppuration is present.

The author's procedure with transillumination intensifies the findings and enables a more precise differential diagnosis. BATSON, Philadelphia.

Miscellaneous

CLINICAL OBSERVATIONS ON EFFECTS OF CHOLINE COMPOUNDS IN NEUROLOGIC DISORDERS, WITH SPECIAL REFERENCE TO MÉNIÈRE'S SYNDROME. MELBOURNE J. COOPER, Am. J. M. Sc. **195**:83 (Jan.) 1938.

Six patients with Ménière's syndrome classified on the basis of arteriosclerosis or vasospasm were treated orally with an average of from 0.006 to 0.008 Gm. of ethylbetamethylcholine hydrochloride three times a day. They were observed in a total of fourteen severe and two minor exacerbations. Five obtained satisfactory relief from the vertigo, headache, ataxia and nausea. The continued use of choline during intervals of quiescence usually, but not invariably, appeared to prevent the recurrence of exacerbations. No tolerance developed after prolonged administration of the drug. One patient having major trigeminal neuralgia was relieved by taking the drug orally in doses of 0.0166 Gm. three times a day. Another patient with marked peripheral arteriosclerosis and intermittent claudication obtained relief while taking choline preparations.

MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

CONTRACTIONS IN DENERVATED MUSCLES OF MONKEYS INDUCED BY FRIGHT AND REPRODUCED BY ACETYLCHOLINE. MORRIS B. BENDER, Arch. Neurol. & Psychiat. **39**:421 (Feb.) 1938.

The author states that numerous studies have shown that the action of autonomic nerve fibers is through the medium of specific chemical changes. Epinephrine is liberated during emotional stress. The liberation of acetylcholine during fright has not been demonstrated, though there are signs of parasympathetic activity. The contraction of denervated muscle in contact with acetylcholine can be used as an indicator in the detection of acetylcholine. Bender made use of this knowledge in his experiment on monkeys whose facial and ocular muscles were completely paralyzed by section of the facial nerve. After degeneration of the nerve endings had taken place, the monkeys were angered or frightened. Contractions of the paralyzed muscles were observed in every animal tested, so long as the muscles remained denervated. The contractions were invariably augmented with physostigmine, could be reproduced by intramuscular injections of physostigmine and acetylcholine and were produced by intravenous injection of acetylcholine. Atropine had no effect, while epinephrine inhibited the contractions.

The author states that his results suggest that contractions in denervated muscles induced by fright are due to a substance secreted in the body which is

similar in action to acetylcholine. Stimulation or resection of the cervical portion of the sympathetic chain or of the infraorbital nerve had no visible effect. Neither extirpation of the superior cervical ganglion, even bilaterally, nor resection of both facial nerves and of the ipsilateral oculomotor and trochlear nerves had any effect.

Quoting from the literature, the author states that acetylcholine could not be demonstrated in the blood after stimulation of the vagus nerve. However, this fact does not detract from the possibility that during fright, when the entire organism is strongly activated, an excess of an acetylcholine-like substance is secreted in all parts of the body, some getting into the general circulation and reaching the sensitized denervated muscle. Other experiments have shown that the higher the animal is in the phylogenetic scale, the less conspicuous are the contractions in denervated muscles induced by fright or reproduced by acetylcholine.

Whether acetylcholine is formed locally or reaches the denervated muscles through the general circulation, the experiments indicated that acetylcholine is secreted during fright; the author suggests that during fright there is a general discharge of the autonomic nervous system and secretion of sympathetic and parasympathetic hormones for protection of the organism.

VAIL, Cincinnati.

HUMAN AUTONOMIC PHARMACOLOGY: XII. THEORIES AND RESULTS OF AUTONOMIC DRUG ADMINISTRATION. ABRAHAM MYERSON, J. A. M. A. **110**:101 (Jan. 8) 1938.

Myerson reports the results of his research on drugs which are specific in their action on the autonomic nervous system. In a discussion of the balance between the sympathetic and the parasympathetic system (the anatagonism between acetylcholine produced by the parasympathetic nervous system and the elements called sympathin E and I produced by the sympathetic nervous system), he states "since the sympathins are more or less like adrenin, the chemical concept of balance may be stated as the resultant of the effects of cholinergic and adrenergic substances." Choline-esterase, described by Stedman, is believed to hydrolize or destroy acetylcholine, but at the present time there is no known antagonist to sympathin. The question as to whether there are substances antagonistic to sympathin cannot be answered until sympathin has been isolated. Myerson believes that the concept of balance between the sympathetic and the parasympathetic system does not explain all autonomic functions, as there are some organs which have only one set of innervating structures; there are functions of organs which respond to only one type of drug, and there are other structures, such as the sweat glands, which are anatomically innervated by the sympathetic system alone but mainly cholinergic in chemical function. He submits a working hypothesis of human autonomic pharmacology, showing the adrenergic action of epinephrine and benzedrine, the production of acetylcholine in the synapses of both the sympathetic and the parasympathetic system and the checking of acetylcholine by esterase, which in turn is destroyed by physostigmine and prostigmine (dimethylcarbamic ester of m-oxyphenyl trimethylammonium methylsulfate). Thus the action of acetylcholine and mecholyl (acetylbetamethylcholine hydrochloride) is enhanced. Myerson summarizes the effects of mecholyl, benzedrine sulfate, atropine sulfate and prostigmine as follows:

From 2 to 10 per cent mecholyl dropped into the conjunctival sac constricts the pupil; the physostigmine and prostigmine which inhibit the esterases constrict the pupil. Atropine, scopolamine and stramonium, which inhibit the action of acetylcholine, abolish constriction. Dilatation follows the use of the adrenergic drugs epinephrine and benzedrine.

A balanced reaction of the iris to light until complete miosis is permitted by the cholinergic substances, whereas atropine inhibits the reaction and benzedrine diminishes it in proportion to the strength of the instilled solution.

Intraocular tension, in part a balanced autonomic function, is diminished by the instillation of mecholyl and by prostigmine and physostigmine. This effect is

abolished by atropine, which increases tension. Benzedrine increases intraocular tension, while benzedrine plus atropine is decidedly synergistic.

The ciliary muscle anatomically is exclusively parasympathetic, and mecholyl increases accommodation of the lens, an effect likewise produced by the instillation of physostigmine or of prostigmine; a combination of prostigmine and mecholyl gives a marked effect. Atropine prevents this reaction. Benzedrine would be expected to have no effect on accommodation, since it is a sympathomimetic drug, but actually it tends to disturb the accommodation of the lens in the same way that atropine does.

"The production of sweat is a cholinergic function, although sympathetic in innervation. Mecholyl and pilocarpine cause marked alkaline general sweating. Localized sweating can be brought about by intradermal injection. This effect is greatly enhanced by prostigmin, although in itself this drug produces no sweating. Atropine abolishes or prevents these effects. Epinephrine and benzedrine have no effect in ordinary doses on the sweating."

Myerson discusses the effects of these drugs on the circulation, the gastrointestinal tract and the gallbladder.

His comment is rather important and for that reason is quoted in full:

"*Comment.*—In using these drugs, namely, mecholyl, benzedrine, prostigmin and atropine, certain definite and general principles must be kept in mind. Any increase in the amount of prostigmin used renders mecholyl enormously effective and to the point of danger to the patient. A dose above 1 mg. of prostigmin makes it undesirable to use mecholyl in any amount above 5 or 10 mg. A safer dose of prostigmin is 0.5 mg. (These figures apply only to intramuscular injection; the use of prostigmin by mouth has a wider range of safety.) Moreover, atropine should always be held in readiness whenever mecholyl is to be used alone therapeutically or experimentally. Practically speaking, there is no danger, no matter what the effect of mecholyl may be, if atropine is used intravenously or intramuscularly in sufficient dose. The administration of one-fiftieth grain (0.0013 Gm.) intravenously blocks, practically speaking, all effect of mecholyl.

"If, however, prostigmin is used in addition to mecholyl, atropine is not sufficient to check the effects. Evidently the choline-esterase and atropine are synergistic so far as blocking the effects of mecholyl is concerned. Consequently, whenever the esterases have been removed as a buffer to mecholyl by the use of prostigmin, it is advisable to add epinephrine, benzedrine or, better still, the combination of the two, to the atropine. With such treatment the ill effects of excessive doses rapidly disappear.

"It is probable that the electric current will furnish an important and useful way of introducing mecholyl for therapeutic purposes. In cases of gastro-intestinal disease and in the experiments carried out on blood pressure, it has been possible to maintain a mild general effect for hours, so that, for example, the juices of the stomach became definitely alkaline and mucous without any profound disturbances of blood pressure and heart rate and without the creation of marked general sweating.

"It is to be kept in mind that benzedrine and atropine are synergists and that when the combination is used the dose of each drug must be reduced in order to get any beneficial effects without too many untoward results. The mood effects of benzedrine are best produced by small doses, and in many cases 2.5 mg. two or three times in the morning will produce far better results than large doses. In fact, it may be stated that the mood effects occur beneath the threshold at which the visceral changes take place.

"These experiments also indicate that it is possible by pharmacologic experiment to reproduce many of the so-called symptom complexes. Thus, achylia gastrica is simulated by the action of mecholyl. Heart block can be readily produced by prostigmin and mecholyl. The spastic condition of the colon, as well as the atonic one, can be reproduced by the use of mecholyl and benzedrine, respectively. If sufficient prostigmin is used, the presbyopic eye can be transformed for a time

into the myopic eye. In other words, the gradually developing theory that repeated functional disturbances may eventuate into organic disease has at least a working basis in the effects of these drugs.

"Perhaps the most novel general implication is the emphasis to be laid on the esterases. These products of bodily activity have an important role in the regulation of cholinergic or parasympathetic activity. There may be, and it seems likely that there are, conditions of hyperesterasia, that is to say, situations in which the esterases are present in too great a quantity to permit the free working of the acetylcholine produced by the body. This might well be the case in presbyopia. On the other hand, there are conditions in which hypoesterasia may be postulated, as when there is hyperactivity of cholinergic type or of parasympathetic origin. Heart block might thus be interpreted. It will be necessary to isolate the esterases before this hypothesis can be tested against fact."

H. H. Vail, Cincinnati.

Filtrable Viruses in Infection of the Upper Respiratory Tract. A. R. Dochez, Katherine C. Mills and Yale Kneeland Jr., J. A. M. A. **110:** 177 (Jan. 15) 1938.

Dochez and his co-workers present a summary of the researches which have been carried out in several laboratories during the past decade. A large series of transmission experiments have demonstrated that there exists in connection with the common cold a filtrable virus, which in all probability may be the primary etiologic agent and can interact with the various pathogenic agents of the upper part of the respiratory tract to produce more severe infections. Numerous observations during such experiments seem to indicate that the uncomplicated cold in adults is practically a pure virus disease. Another series of experiments by the same group led them to conclude that a filtrable virus had been recovered from patients with interpandemic influenza. In 1933 the influenza problem was approached from another angle. The authors were able to obtain several strains of the virus, which is pathogenic for ferrets. These were obtained from patients with typical attacks of influenza. Once established in the ferrets, the disease can be transmitted to white mice, in which after a few passages it produces fatal pneumonia. Immunologic studies performed with these various serums seem to show that strains of influenza virus from different parts of the world are similar.

Attempts to initiate a transmissible virus disease in ferrets with material derived from persons with a common cold (except typical influenza) have been failures. The evaluation could therefore be made as follows: The primary etiologic agents of certain acute infections of the upper part of the respiratory tract seem to be filtrable viruses; the fact that virus from patients with severe influenza is pathogenic for ferrets and can be cultivated best in aerobic mediums, while virus from patients with colds or related infections is not pathogenic for ferrets and has been cultivated only under anaerobic conditions, suggests that at least two different types of filtrable virus exist, the cold virus and the virus of epidemic influenza. Preliminary studies with immune serums showed an immunologic dissimilarity between cold virus and influenza virus, but these experiments were interrupted because a new and highly fatal virus appeared. This new virus was later observed to be present occasionally in the lungs of apparently normal mice and to undergo a rapid enhancement of virulence on repeated intranasal passage. Great caution is necessary in interpreting results obtained with such a technic. Attempts to develop immunity by subcutaneous injections of the living virus in chimpanzees were encouraging but failed in the several groups of human beings. Whether this failure could be attributed to the existence of a multiplicity of strains of virus, to the impossibility of preparing virus in large quantities free from the constituents of the nutrient medium or to the possibility that resistance to colds is a purely local rather than a general bodily phenomenon is uncertain at the present time.

In the discussion, Dr. M. L. Blatt, of Chicago, said that it is necessary to define accurately just what the common cold is. In the field of pediatrics one finds other diseases diagnosed as the common cold. They are allergies to food, pollen or bacteria, old sinus infections and rhinorrhea brought on by exposure to drafts or cold (the so-called histamine type). One of the greatest difficulties in the careful evaluation of vaccination with virus against the common cold will result from the difficulty in diagnosis. With influenza, however, the picture is quite different. The disease is a recognized entity. GORDON, Philadelphia.

PROFESSOR PORTMANN'S 1937 COURSE. Rev. de laryng. **59**:1 (Jan.) 1938.

Professor Portmann's 1937 course was given at the medical school at Bordeaux and in the clinics of La Glaciere Hospital in Paris. The title is somewhat misleading in that the article is in effect a description of the work offered in 1938. It is really an announcement of the annual course. These courses are given in both French and English. The article should be consulted by those interested in study with Dr. Portmann. No doubt, the same information could be obtained from Dr. James Flynn, Georgetown University Medical School, Washington, D. C., who is the president of the Alumni Association. BATSON, Philadelphia.

NEW COMMENTS ON THE ABNORMAL HYOID APPARATUS. P. MANGABEIRA-ALBERNAZ, Rev. de laryng. **59**:187 (Feb.) 1938.

Abnormalities of ossification of the hyoid apparatus occurred in 14 per cent of the 464 persons examined. The incidence was almost equally divided between the two sexes. While ossification of the cartilages increases with age, these studies indicate that abnormal ossification of the hyoid apparatus is in the nature of a congenital anomaly and not due to a simple, slow ossific process as described by most of the modern authors. BATSON, Philadelphia.

PROPHYLACTIC TREATMENT OF CERTAIN COMPLICATIONS ATTENDING OTORHINOLARYNGOLOGIC OPERATIONS. H. LEWENFISZ, Rev. de laryng. **59**:200 (Feb.) 1938.

The intramuscular injection of acetylarsan (parahydroxyacetylaminophenylarsinate of diethylamine) on the day of such otolaryngologic operations as, for example, tonsillectomy and operations on the sinuses is recommended. The author believes that a decrease of postoperative complications and greater comfort to the patient result from the bactericidal action of the organic arsenic compounds on the spirilla and fusiform bacilli commonly found in the mouth.

BATSON, Philadelphia.

Directory of Otolaryngologic Societies *

FOREIGN

Collegium Oto-Rhino-Laryngologicum Amicitiæ Sacrum

President: Dr. Louis Ledoux, Brussels, Belgium.
Secretary: Prof. Dr. C. E. Benjamins, Verlengde Heereweg 143, Groningen, Netherlands.
Place: Brussels, Belgium. Time: September 1939.

Hungarian Otolaryngological Society

President: Dr. J. Treer, Bocskay-u. 9, Szeged.
Secretary: Dr. G. Kelemen, Reáltanoda-u. 9, Budapest.

Sociedad Rioplatense de Oto-Rhino-Laringología (Argentine Section)

President: Dr. Raul Becco, B. Mitre 1690, Buenos Aires.
Secretary: Dr. Juan Manuel Tato, Santa Fé 1171, Buenos Aires.

Société Française d'Oto-Rhino-Laryngologie

Secretary: Dr. Henri Flurin, 19 avenue Mac-Mahon, Paris (17°).

NATIONAL

American Medical Association, Scientific Assembly, Section on Laryngology, Otology and Rhinology

Chairman: Dr. H. Marshall Taylor, 111 W. Adams St., Jacksonville, Fla.
Secretary: Dr. Leroy A. Schall, 270 Commonwealth Ave., Boston.
Place: St. Louis. Time: May 15-19, 1939.

American Academy of Ophthalmology and Otolaryngology

President: Dr. George M. Coates, 1721 Pine St., Philadelphia.
Executive Secretary: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Place: Chicago. Time: Oct. 8-13, 1939.

American Bronchoscopic Society

President: Dr. John D. Kernan Jr., 120 E. 75th St., New York.
Secretary: Dr. Lyman Richards, 319 Longwood Ave., Boston.
Place: Westchester Country Club, Rye, N. Y. Time: May 27, 1939.

American Laryngological Association

President: Dr. George B. Wood, 504 Physicians' Bldg., Philadelphia.
Secretary: Dr. James A. Babbitt, 1912 Spruce St., Philadelphia.
Place: Westchester Country Club, Rye, N. Y. Time: May 24-26, 1939.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Harold I. Lillie, Mayo Clinic, Rochester, Minn.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester, N. Y.
Place: Drake Hotel, Chicago. Time: May 9-11, 1939.

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* Secretaries of societies are requested to furnish the information necessary to keep this list up to date.

SECTIONS:

Eastern.—Chairman: Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H.
Southern.—Chairman: Dr. Francis E. LeJeune, Maison Blanche Bldg., New Orleans.
Middle.—Chairman: Dr. T. R. Gittins, Davidson Bldg., Sioux City, Iowa.
Western.—Chairman: Dr. Frederic G. Sprowl, Medical Arts Bldg., Spokane, Wash.

AMERICAN OTOLOGICAL SOCIETY

President: Dr. Isidore Friesner, 36 E. 73d St., New York.
Secretary: Dr. Thomas J. Harris, 104 E. 40th St., New York.
Place: Westchester Country Club, Rye, N. Y.: Time: May 22-23, 1939.